INFORMATION

Cases of Poisoning Reported by Physicians

2011–2013

Bundesinstitut für Risikobewertung

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Cases of Poisoning Reported by Physicians 2011–2013

Poisoning and Product Documentation Centre at the Federal Institute for Risk Assessment – 18th Report (2011–2013)

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Preface

Professor Dr. Dr. Andreas Hensel

Dr. Dr. Axel Hahn

Dear Reader,

On 1 August 1990, the requirement of compulsory reporting of cases of poisoning by attending physicians came into force within the framework of the Chemicals Act (Chemikaliengesetz – ChemG). Medical practitioners and physicians in hospitals, but also colleagues not involved in direct treatment of patients such as physicians in public health services or forensic experts who obtain sufficient information on human cases can provide us with valuable data. As intended by legislation, relevant information should be submitted timely, i.e. also in reasonably suspected cases of poisoning to ensure that effective measures of prevention and therapy can be recommended at a very early date.

The authors take great pleasure in publishing and offering to you the latest, that is the 18th Report by the Poisoning and Product Documentation Centre. In addition to the recording, assessment and documentation of cases of poisoning, our Centre at BfR is also entrusted by legislation with the recording of product formulations, which are made available to the German poison information centres. In recent years, there has been a noticeable increase in the number of such product notifications. As a result, the workload for the Centre's Team has grown considerably. This is why the present report on Cases of Poisoning Reported by Physicians has been prepared as a 2011– 2013 cumulative volume, i.e. there is no time gap between the current and the previous 2010 report.

We would like to thank everybody for the great interest shown in our brochure and the numerous enquiries submitted regarding the date of publication of the next report on Cases of Poisoning Reported by Physicians. Awareness of the topic of poisoning will benefit, on the one hand, a targeted poison information and treatment of patients in cases of poisoning, and on the other, a continuous improvement of product safety for consumers. The particular

value of our reports lies in their topicality, i.e. the description of cases of poisoning actually observed. This is also reflected by the fact that our case reports are gladly used for teaching at universities.

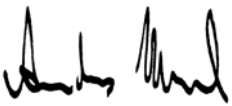
As demonstrated by the results achieved so far in assessing cases of poisoning, it is not appropriate to derive assessment data of chemical substances on the basis of animal studies alone. This has been impressively confirmed by the example of lamp oils and grill lighter fluids containing paraffins or petroleum: Standard animal experiments had not indicated any hazard. However, when the popularity of ornamental lamps with coloured and scented lamp oils had rapidly increased in Germany, a rise in the incidence of chemical pneumonia due to lamp oil ingestion was observed in parallel, and even single fatal cases occurred.

Soon thereafter, regular enquiries among physicians, poison information centres and hospitals were conducted by the Poisoning and Product Documentation Centre. These enquiries initiated a process which has resulted in new findings about the epidemiology of health risks from hydrocarbons posing an aspiration hazard, the accident mechanism, the special physicochemical properties and the resulting pathophysiological mechanisms of pulmonary aspiration and aspiration pneumonia. It was found that the toxicity of liquid petroleum distillates and paraffins had been underestimated, on the basis of the results of standard animal experiments available at that time.

As in the cases of dangerous lamp oils and grill lighter fluids, the nitric acid-containing product, Por Çöz in 2009 or the Magic Nano case series in 2006, the BfR Poisoning and Product Documentation Centre has identified new risk potentials for human health based on the assessment and evaluation of cases of poisoning, and such activities resulted in corresponding European regulations. This has demonstrated that a dedicated monitoring and scientific assessment of products for adverse effects, based on the Cases of Poisoning Reported by Physicians, are well suitable to effectively reduce risks in a sustainable manner.

The eight (2015) German poison information centres receive about 220 000 enquiries on poisonings every year. This indicates that it would be important for early risk identification and absolutely necessary for an effective legislation to establish a national monitoring of poisoning incidents similar to that already existing e.g. in the United States of America. The basic features of such monitoring activities are currently being developed by the National Committee for the Assessment of Poisonings at BfR, that celebrated its 50th anniversary in 2014.

Among our readers, attending physicians, staff of poison information centres and patients have been and will be the most important sources for an accurate and correct documentation of poisoning incidents. Therefore, we would be grateful for your active support also in the future.



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The Federal Institute for Risk Assessment

Do nanoparticles promote the development of allergies? Does apple juice contain harmful aluminium? The Federal Institute for Risk Assessment – in short BfR – is responsible for questions to do with the health assessment of food, consumer products and chemicals. In its work it makes an important contribution to rendering food, products and the use of chemicals safer in Germany.

BfR was established in November 2002 to strengthen consumer health protection. It is the scientific body of the Federal Republic of Germany that prepares expert reports and opinions on questions of food and feed safety and the safety of substances and products. In doing so, the Institute assumes an important task in improving consumer health protection and food safety. The activities of the BfR are conducted under the responsibility of the Federal Ministry of Food and Agriculture. At the three BfR locations in Berlin, a staff of about 770, among them 300 scientists, is being employed to work in the field of consumer health protection. The scientific expertise needed for its assessment and research activities is provided on a non-partisan basis.

In our globalized world it is important for the institutions involved in consumer health protection to be part of international networks. The BfR is the national Focal Point of the European Food Safety Agency (EFSA) and a partner of the European Chemicals Agency (ECHA). It cooperates with a number of national and international, governmental and non-governmental agencies.

The BfR sees itself as the advocate of consumer health protection in a context in which many stakeholders make their voices heard. On the scientific basis of its risk assessments, it seeks to strengthen consumer health protection.

To this end, the Institute participates in national and international panels, offers policy advice and disseminates consumer information. Risk communication has been provided by BfR by means of various events and projects. Thanks to the high standard of its work, its scientific independence and its transparent assessments, the Institute has become a recognised player and important driver of consumer health protection on both the national and international stage. Consumers know they can trust its judgements.

→ **www.bfr.bund.de**

1 Introduction

1.1 Legal basis of activity: § 16e Chemicals Act

On 1 August 1990, the requirement of compulsory reporting of poisonings by attending physicians within the framework of the Chemicals Act (Chemikaliengesetz – ChemG) came into force. This compulsory reporting is a counterpart to the reporting of adverse reactions to medicinal products (pharmacovigilance). In addition to compulsory reporting of cases of poisoning, the requirement of notification of dangerous chemical products (dangerous mixtures) was introduced at the same time. Poison information centres had to undertake to report their relevant knowledge of the situation with regard to poisoning incidents in Germany. All these activities merge at BfR at the Poisoning and Product Documentation Centre, where also the secretariat of the BfR Committee for the Assessment of Poisonings is hosted.

It has been an objective of this legal provision in the German Chemicals Act to receive from physicians well documented findings on health impairment in humans caused by chemical products. It serves to provide valuable data on the incidence of poisoning accidents, doses and effects of chemicals and products in humans. On the basis of such data, effective measures of prevention can be recommended at a very early date (toxicovigilance). The specific intention of legislation was that the toxicological assessment of chemical substances and products should not rely on toxicological data from animal studies alone. The data obtained from cases of poisoning in humans are intended to be used as far as possible to minimise toxicological studies in animals and thus, make an active contribution to animal welfare.

The reporting and systematic evaluation of cases of poisoning represents a legal provision that is useful for both humans and animals and unique on the global level. The cases of poisoning reported by physicians have been compiled, assessed and evaluated at BfR in direct cooperation with attending physicians and the German poison information centres for more than 20 years now. The reports being published in a German as well as an English version have met with a most affirmative response among the scientific community owing to their dealing with toxicological issues of current interest, proposals for preventive measures and the presentation of individual case reports.

In addition, ministries, companies and industrial associations are informed about adverse effects of chemical products through a well-working product information system (PRINS) either immediately by rapid communications (in severe cases of poisoning) or at annual intervals by summary reports (in all other cases).

Compulsory reporting

According to the Chemicals Act, reporting refers to illnesses or suspected poisonings as well as cases of unintentional exposure associated with the following substances or toxic agents:

- Chemical substances and products used in the household, e.g. detergents and cleansing agents, hobby and DIY articles;
- Cosmetics
- Detergents and cleaning agents;
- Pest control products;

- Plant protection products;
- Wood preservatives;
- Chemicals used at the workplace;
- Dangerous chemical substances present in the environment, including those released during industrial accidents;
- Poisonous plants including mushrooms; and
- Poisonous animals.

Who is to report?

Compulsory reporting of substance-related diseases is intended to enable a realistic assessment of health risks posed by individual substances, particularly with regard to acute illnesses, based on representative substances. This is why physicians are obliged to report to BfR diseases or sequelae of diseases possibly attributable to exposure to dangerous substances, chemical products or products releasing or containing dangerous substances. The report should contain information on the substance or product involved, the route of exposure, the quantity absorbed, symptoms and signs as well as the patient's age and sex. Any information about the patient is to be submitted in anonymized form. The reports can be submitted by ordinary mail, e-mail or fax.

1.2 What does the term "poisoning" mean?

The term, poisoning, refers to illnesses caused by exposure of the human body to chemical substances or products and determined by their chemical and physical properties. In the majority of cases, the substances involved are not single ones but chemical products composed of a number of single substances in the sense of a formulation. For many poisons of animal or plant origin, full knowledge of their specific toxic effects is still lacking. Therefore, toxicological research into these effects must continue.

The practice of human toxicology, i.e. the science dealing with the effects of toxic substances in humans, requires special knowledge and a long-standing experience. This applies in particular to the assessment of cases of poisoning. For the assessment of cases of poisoning in humans, toxicological findings and knowledge obtained from animal studies may be helpful to a limited extent only.

Within the meaning of the Chemicals Act, the term of poisoning designates all such cases in which health impairment has occurred. Reporting is also required for suspected cases of poisoning. Poisoning may occur through a variety of routes of exposure to a product, e.g. after oral or inhalation exposure or after contact with the eyes or the skin.

Health impairments in the sense of adverse effects or allergic reactions occurring during or after the customary use of a product are to be reported to BfR, irrespective of the proper or improper use. BfR may also be informed of accidents involving a product which did not result in any health impairment (asymptomatic cases). Information on asymptomatic cases with documented exposure may provide useful information with regard to a risk potential and help define the safety range of the use of a product.

In addition, poison information centres are legally obliged to inform BfR about occurrences of general importance that have come to their knowledge so that trends may be identified at an early date and considerations made with regard to preventive action.

1.3 Principles of clinical toxicology

The assessment of cases of poisoning is based on the established principles of clinical toxicology in the sense of an expert judgement. The following queries have to be answered.

- Does the patient suffer from a disease or condition showing manifestations that can be clearly described?

PSS grade		German (BfR)	
0	none	keine	no symptoms or signs
1	minor	leicht	mild, transient and spontaneously resolving symptoms or signs
2	moderate	mittel	pronounced or prolonged symptoms or signs
3	severe	schwer	severe or life-threatening symptoms or signs
4	fatal		death

Table 1: Poisoning severity score (PSS): International standardized severity grading of health disorders in cases of poisoning

- Is there any evidence existing or to be established that exposure to specific substances or products has taken place? Is it possible to confirm such exposure by laboratory evidence?
- Is there any evidence of an association, i.e. a causal relationship between the condition or manifestations, respectively, and the exposure?

1.4 Standards for the assessment of poisonings

A systematic, uniform and harmonized documentation of reports of cases of poisoning by physicians and their assessment are the essential prerequisites for adequately confirmed and timely hazard identification. All single reports by physicians are recorded in a standardized and harmonized way.

As in all other fields of medicine (e.g. assessment of cases in occupational medicine), cases of poisoning must be assessed on the three different assessment levels described above, guided by objective criteria. For the medical assessment of a case, it has been particularly helpful to consider the individual manifestations as entities in their own right where the degree of severity of the health disorder is weighted correspondingly. This will provide a clear basis for the assessment by differential diagnostic considerations.

For the assessment of cases of poisoning by BfR, standardized instruments are available, which were either adopted and modified or developed at the institute. These instruments have been described in detail in the 2009 annual report. For details, see Annex 6.1 to this brochure. The degree of severity of manifestations (symptoms and signs) and conditions is assessed on the basis of the international poisoning severity score (PSS)[1] (see Table 1).

The most important element for the assessment of both acute and chronic poisonings is the BfR three-level model presented in Chapter 6.1.1, Fig. 35. It was developed in analogy to the assessment of the causal relationship in the recording of adverse effects of medicinal products to enable a differentiated assessment of individual cases of health impairment from poisoning. The advantage of the BfR three-level model assessment consists in a reduction of assessment efforts to three single levels which are logically interconnected.

- Is there a justifiable temporal and spatial association between the exposure and the occurrence of health impairment?

1 *Persson, H.E., Sjöberg, G.K., Haines, J.A., Pronczuk de Garbino, J. (1998) Poisoning Severity Score. Grading of acute poisoning. Clinical Toxicology 36 (3): 205–213.*

- Are the signs and symptoms known from other case reports, or can they be explained on the basis of the mode of action?

- Is there an association between symptomatology and exposure, i.e. are the symptoms and signs temporally associated with dechallenge (symptomatology subsiding after termination of exposure) or rechallenge (symptomatology aggravating on re-exposure)?

The assessment of exposure and health disorders/manifestations is supported by two BfR matrix models, i.e. a model to determine the degree of probability of exposure (Chapter 6.1.2, Table 11) and another one to assess the causal relationship between health disorder/manifestations and exposure (Chapter 6.1.3, Table 12).

1.5 Procedure of assessment and risk communication

The reports received on health impairments associated with chemicals are subjected to an assessment procedure. The causal relationship between the toxic agent absorbed and the symptomatology observed can be classified as “none”, “possible”, “probable”, “confirmed”, “cannot be assessed” or “improbable”.

The estimation of toxic risks for humans is based on differentiated analyses and assessments. For these purposes, the data on cases in humans are continuously documented in the form of case data sets and case reports. Information on identified risks is passed on to the responsible ministries, manufacturers and industrial associations in the form of rapid communications or to the manufacturers in the form of annual summarizing reports disseminated by way of the product information system PRINS (see Chapter 5.3). The responsible manufacturers and/or distributors are requested to transmit to BfR information on measures envisaged by them to improve product safety. The knowledge gained during this process is published by BfR in its reports entitled Cases of Poisoning Reported by Physicians. The latter can be ordered or downloaded via the Internet at www.bfr.bund.de.

For a summary of the terms of reference of the BfR Poisoning and Product Documentation Centre and the respective procedures, please refer to Fig. 36 in Annex 6.2.

1.6 Toxicological history

The case history is one of the most important elements of information to be obtained by a physician on a patient’s condition, forming the essential basis for a plausible assessment of a case of disease. For this purpose, a general case history will comprise at least seven parts:

1. Elucidation of current complaints with special reference to the temporal development of the patient’s condition;
2. Previous diseases and medical examinations;
3. Differential diagnostic considerations;
4. Medical history provided by persons other than the patient (sometimes referred to as heteroanamnesis);
5. Family history;
6. Social history; and
7. Travelling history.

In general, toxicological health impairments should be dealt with according to the same principles as for medical conditions of general character. However, items 4 to 6 are of minor importance as compared to a general medical history.

For a specific toxicological case history, a number of other facts are of particular importance. These include:

1. The routes of exposure (oral, dermal, inhalational etc.);

2. The dose and duration of exposure (acute/chronic);
3. The toxic agent(s) having caused the health impairment; and
4. The spatial and temporal relationship between the toxic agent(s) involved and the manifestations observed.

An accurate and plausible toxicological assessment of the health impairment observed should be preceded by elucidation of the special toxicological data.

Routes of exposure (oral, dermal, inhalational etc.)

For any type of health impairment due to toxic agents it is important to take special account of the route or path of exposure. In many cases, substances are ingested by mistake (oral route of exposure). Inhalation is the route of exposure second in frequency in cases of poisoning. Exposure through the skin, i.e. the dermal route, ranks third in frequency. Often, the routes of exposure are combined, e.g. oral and inhalation or oral and dermal route. Quite frequently, above all in occupational accidents, but also in those affecting children, it is dermal exposure that leads to health impairment, particularly if clothing contaminated after spillage of substances or products is not removed early enough. Depending on the duration of exposure, considerable quantities may be absorbed, particularly after previous damage to the skin barrier due to contact with irritating or corrosive substances.

Dose and duration of exposure (acute/chronic)

Almost without exception, it is very difficult to make a precise estimate of the dose absorbed unless sufficient evidence is provided by direct observations (e.g. two sips of a liquid or differences in quantities of substances kept in transparent vessels). This is especially difficult in cases of exposure by inhalation, particularly if taking place outdoors. The doses released and absorbed by inhalation will depend on a variety of parameters (room size, room furnishings, ventilation, temperature etc.) and on the direction of spreading. Outdoors, the latter will be determined to a considerable degree by the meteorological conditions (e.g. wind speed and direction). There are no reliable calculation methods available at present. Thus, also specialists have to rely on estimates, which most often will be based on a worst case scenario.

Toxic agent

For the assessment of health impairments due to chemical products such as household products, paints, lacquers/varnishes, glues, insecticides etc., it is important to undoubtedly identify and document the responsible substance or product on the one hand and the resulting symptomatology, on the other. For a differentiated assessment of health effects it is also important to identify the dynamics and severity of the manifestations observed, in addition to the dose and route of exposure.

In this context, unequivocal identification of the responsible product is the most important information to be obtained by the attending physician. Based on the experience gained so far this means that for an assessment of health risks involved it is imperative for the attending physician to know not only the correct product or trade name of a product but also its current formulation.

1.7 Poison information database

The BfR poison information database serves to support the poison information centres in providing consultation and treatment in cases of poisoning by making available product formulations notified by manufacturers/distributors for purposes of emergency health response.

To this aim, industry is obliged to supply BfR with information on chemical products that have been classified as dangerous. In addition, BfR receives product notifications on biocides,

detergents and cleaning agents. The legal basis for such notifications is provided by § 16e para 1 of the Chemicals Act (Chemikaliengesetz – ChemG), and § 10 of the Detergents and Cleaning Agents Act (Wasch- und Reinigungsmittelgesetz – WRMG). Until 2007, BfR also received notifications of formulations of cosmetics.

In addition, companies may, on a voluntary basis, provide BfR with information on products not subject to the requirement of notification to enable fast and competent advice by a poison information centre in cases of accidents.

By the end of December 2013, a total of 182 577 documents containing product information were kept at the BfR product database. Of these, 95 593 are new notifications of products that were added in the 2011 – 2013 period.

In 2007, the Detergents and Cleaning Agents Act stipulated for the first time that these data should be submitted to BfR in electronic form. To this purpose, BfR had developed an XML data exchange format (XWRMG), which has shown an excellent performance. In its wake, another electronic data exchange format (XProductNotification) was made available to the companies free of charge permitting computerized notification of all products (both notifications on a legal as well as on a voluntary basis). Already at present, the majority of product notifications are received by BfR in electronic form. The corresponding formats and add-ons are available for downloading from the BfR homepage at www.bfr.bund.de/en/notifications_of_formulations-10144.html .

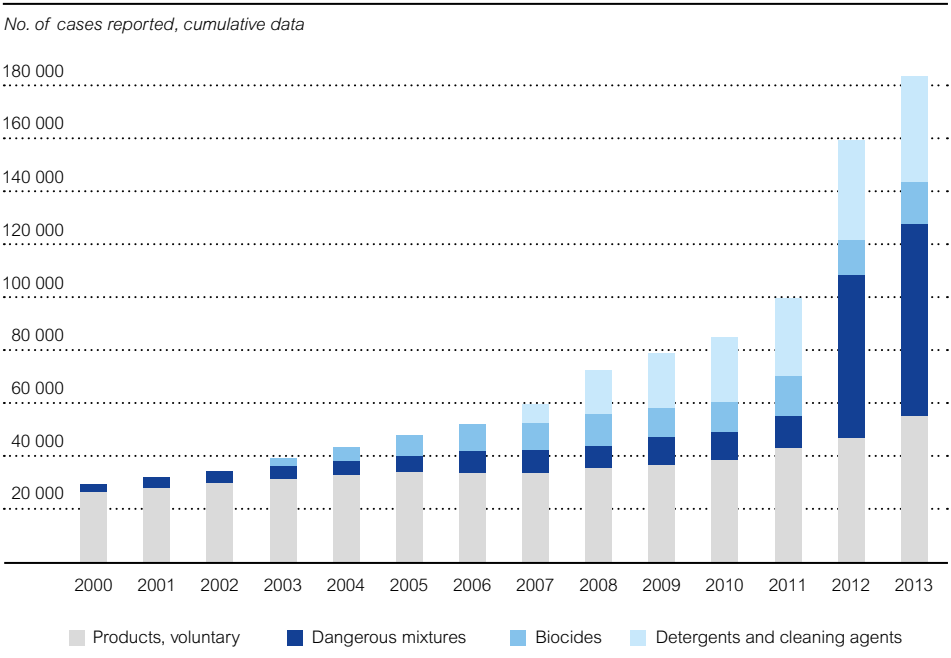

Fig. 1: Product data transmitted to German poison information centres since 2000

All product data notified are edited by BfR and then transmitted to the poison information centres. This procedure has been carried out in electronic form for many years. The legal framework for the notification of formulations is provided by different legal acts (Chemicals Act, Regulation on Biocides, Cosmetics Regulation, Detergents and Cleaning Agents Act). They serve the purposes of consumer health protection and in most cases, have resulted from implementation of European regulations.

Fig. 2: Fourth BfR user conference

1.8 The new Chemicals Act – extended notification requirements for products

On 9 November 2011, the amended Chemicals Act became effective in Germany, harmonizing national law with the requirements of European legislation (CLP Regulation). Beginning with this date, the product notification requirements have been considerably extended. From now on, notification is required for all products classified as dangerous, including e.g. consumer products labelled as irritant or highly flammable. For the first time, notification will also cover all dangerous industrial products which have been frequently involved as toxic agents in occupational accidents/poisoning. As a rule, cases of poisoning of this type are reported to BfR by legal accident insurance companies. There are transitional provisions intended to make it easier for companies to enter into the notification process (e.g. the temporary notification by means of safety data sheets). Under the Chemicals Act, the transitional period will expire in 2016. However, depending on the current state of the European harmonisation process of product notification, which is to be accomplished in parallel to the transitional period, this expiration date may have to be adapted accordingly by German legislation. The harmonisation procedure is intended to result in a product notification on the EU level which is uniform regarding both its form and extent. As an advantage, cross-border notification of formulations would be greatly facilitated. For example, the parameters describing the ingredients to be stated, such as limits of concentration ranges etc., would be uniform for all EU countries. Moreover, it is envisaged to introduce a uniform electronic notification format. For several years already, BfR has been successfully using a defined XML format. In addition, it is planned to introduce a uniform product identifier. This Unique Formula Identifier (UFI) should be printed on the packaging of all dangerous products. It would consist in an encrypted code which in the event of an enquiry received by a poison information centre would enable the latter to rapidly and reliably identify the formulation of the product involved. Altogether, consultants at the centres will have a considerably enhanced set of data at their disposal for an emergency health response in cases of poisoning. Since 2010, a User Conference on Product Notification has been held at BfR at annual intervals. By means of this event, companies, industry, the responsible Länder authorities as well as national and international poison centres are provided an appropriate platform for entering into dialogue with each other.

1.9 Current topics

1.9.1 BfR app for first aid and poison emergency hotlines

In addition to falls, poisoning has been one of the most frequent causes of accidents among infants and young children aged between one and three years. Typical scenarios of poisoning accidents in children include the ingestion of household cleaning products containing surfactants, of body care or medicinal products and plants. Fortunately, most of these incidents have no serious consequences.

Many accidents could be avoided if parents, grandparents, babysitters, childcare workers and teachers were aware of the risks of poisoning and vigilant about preventive measures like keeping such products out of the reach of children. For this reason, BfR has published a brochure on the risk of accidental poisoning in children in 2009 (Risiko Vergiftungsunfälle bei Kindern). It was produced in collaboration with the Berlin poison information centre and the Bundesarbeitsgemeinschaft (BAG) Mehr Sicherheit für Kinder (Safe Kids Germany) and is available free of charge. Due to the enormous demand, BfR has issued an additional Turkish translation of the brochure in 2011. An Arabic translation of the brochure is being prepared at present.

Fig. 3: Risk of Accidental Poisoning in Children – Brochure in German and Turkish

Fig. 4: Instant information by means of the BfR App

In order to raise interest in the topic of poisoning accidents in children also among other target groups by means of a modern medium, an app has been developed at BfR informing about poisoning risks and first aid measures and providing contact with a poison centre as quickly as possible.

The BfR app on poisoning accidents in children provides information about poisoning risks posed by chemical and medicinal products, toys, plants and fungi. The app informs about first aid measures that can save lives in cases of emergency. In addition, it provides knowledge required to protect infants and young children from poisoning. Users will find suggestions about prevention, e.g. on appropriate storage of household and medicinal products. On each product type, the app will provide a list of ingredients and a description of possible symptoms and signs of poisoning. Parents are given advice on action to be taken if their child has become exposed to dangerous substances.

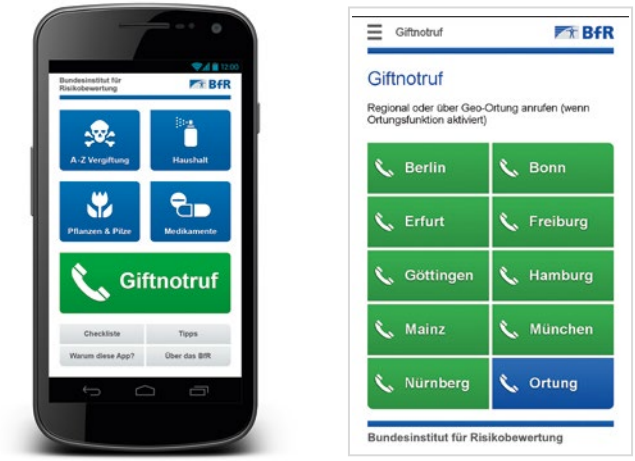

Fig. 5: BfR-App on poisoning in children

The app is an important information and reference guide. In an emergency, an immediate call can be made to the next poison information centre. It is an essential advantage of the BfR app that it can be used immediately after installation on smartphones without internet access. Thus, important information can be obtained at any time and anywhere, whether travelling, staying in a playground, or during a visit to the grandparents

In order to obtain competent advice as quickly as possible, one of the nine German poison information centres can be called directly from the app. By means of a localisation function of the smartphone it is possible to automatically establish a connection with the responsible poison information centre of a German federal Land.

During the development of the app, BfR obtained advice from independent external experts. These included the advisory BfR Committee for the Assessment of Poisonings, whose honorary members support the work of BfR. The Committee has been closely cooperating with the German poison information centres and the corresponding national and international scientific societies.

The BfR app has been developed for all smartphones with Android and iOS operating systems. It is available for free download in the corresponding app stores.

1.9.2 Case report database

1.9.2.1 The BfR case report database

The use of well documented case reports as an empirical case-based research tool has a long-standing tradition in a number of sciences (medicine and law, among others). In this context, case reports have made essential contributions to the development of expert knowledge. In particular, detailed descriptions of extraordinary and unexpected cases of poisoning and the related findings are especially valuable. Specifically, the study of case reports is rated among the “classical” forms of learning in medical science and law and has also played an important role in accident prevention. However, in spite of the legal obligation to report cases under § 16e para 2 Chemicals

Act, there has been a considerable shortage of data in this field still today. So far, Germany does not have any overall statistics on cases of poisoning on the national level. This is a regrettable fact because well documented descriptions of extraordinary and unexpected cases and the related findings could serve as particularly valuable sources to be exploited for enhancing the assessment of cases of poisoning.

For this reason, the compilation of a case report database was launched by BfR as a research and development project in March 2002. In the context of this project, cases of poisoning of particular toxicological relevance and scientific interest (e.g. cases of rare poisonings, cases associated with high-dose or low-dose exposure, cases showing unexpected manifestations and such involving toxic agents of special interest) are processed in a standardized procedure and then recorded and managed in the bilingual BfR case report database (German/English).

Based on approx. 71 000 reports received from physicians, a total of 552 BfR case reports (of which about 80 % have been translated into English) have been prepared in the period from 1 July 2002 to 31 December 2013. The cases prepared in the form of case reports date back as far as 1990. Since November 2011, also posters from international conferences and posters designed by the BfR Poisoning and Product Documentation Unit have been included in the database in order to maintain important empirical data for human toxicology. At international conferences, the BfR case report database has met with great interest. It will initially be published on an internal level, and afterwards, made accessible to a national and international audience of experts. Consequently, making available these well documented and valuable case reports means also a step forward towards an improved assessment of cases of poisoning. The database contains unique data on exposure, the dose-effect relationship in humans (human biomonitoring), the clinical course of illnesses, etc. Furthermore and in line with other conclusions, preventive measures may be developed on the basis of the data collected. Following a test run of about one year, the feedback will be evaluated and potential sources of mistakes will be eliminated and, if appropriate, notes added in a revised version of the case report database. The case report database can be searched both for individual cases and case series. Presently, this project is a unique one because there are no comparable concepts world-wide.

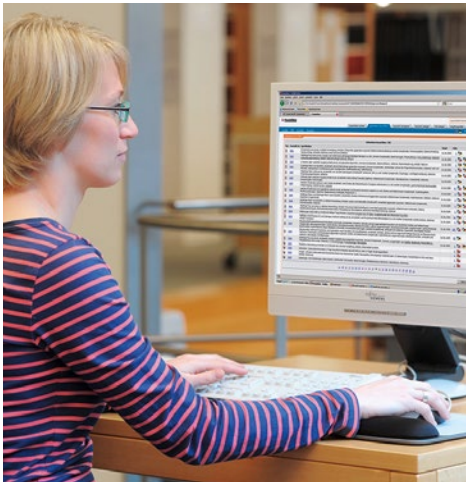

Fig. 6: Practical work with the BfR case report database

The case report database has been in practical use already for internal purposes. The case reports recorded are used for example for rapid communications to ministries (in cases of poisoning suggesting the presence of severe health risks that require immediate action by the responsible authorities), the preparation of BfR annual reports and publications, and of poster presentations both at home and abroad, as well as for scientific lectures at universities as illustrative examples of cases.

The case report database is understood as a continuous exercise. It requires regular maintenance and is subject to constant updating. For the future, it is envisaged to set up a veterinary case database that will constitute the first collection of cases of poisoning in animals. The latter could provide a valuable source of information for veterinary science, animal owners and for educational purposes or serve for comparison with human data. The evaluation of cases of poisoning in animals may provide useful information with regard to a potential risk to human health.

1.9.2.2 The case report database of the BfR as an educational instrument – developments in the treatment of poisoning from chemical products[2]

In an MA thesis, the BfR case report database was used as an educational instrument to describe developments in the therapy of cases of poisoning involving chemical products. For the period between 1 January 1990 and 31 December 2011, these developments were outlined by means of a secondary data analysis and in addition, could be substantiated by scientific findings.

The data volume analysed for this purpose included: All reports of cases of poisoning involving chemical products received by BfR in the period between 1 January 1990 and 31 December 2011 and recorded in the BfR case report database, classified by age groups and sex of the patients affected, and including a review of the therapeutic measures "induced vomiting", "administration of activated charcoal", "administration of laxatives", "gastric lavage" and "administration of an antidote".

Altogether, 55 cases could be reviewed (n = 55). For some of these, duplication occurred resulting from multiple therapies in some cases of poisoning. After adjustment, the number of cases was 34 (nb = 34). In spite of the rather low number of cases considered, a change in the therapy of poisoning could be demonstrated, based on the five therapeutic measures listed above. This was particularly obvious with regard to the first four criteria, "induced vomiting" (→ in the analysis, listed under the search term "ipecac syrup"), "administration of activated charcoal" (→ in the analysis, listed under the search term "charcoal"), "administration of laxatives" and "gastric lavage". It becomes clear that in the 1990s, these therapeutic measures were used much more frequently than in the years after 2000. The peak of cases of poisoning treated with these regimens was found to have taken place between 1992 and 1997.

As compared to these therapies, the group of antidote administration as the fifth criterion has played a distinctive role, showing a chronologically different course. No focussing was seen in the 1990s, but the analysis has shown a consistent share indicating the use of such therapeutic measure over the entire period considered. The antidote proper and its use in treating poisoning involving a specific toxic agent provide information on the historical development. The administration of ethyl alcohol as an antidote in cases of poisoning from ethylene glycol may serve as an example: Since 2006, ethyl alcohol has been replaced by administration of fomepizole as an antidote in these cases. Such changes have also been uncovered by the review. Eventually, it can be concluded that regarding the use of antidotes, historical changes can be identified and scientific progress has been made, on the one hand, while on the other, a number of established antidotes is still being used today (see Fig. 7).

2 *Feistkorn, E. (2012) The Case Report Database of the Federal Institute for Risk Assessment (BfR) as an Educational Instrument – Developments in the Therapy of Cases of Poisoning involving Chemical Products. Available in the libraries of Alice Salomon University (ASH) and BfR Unit 32.*

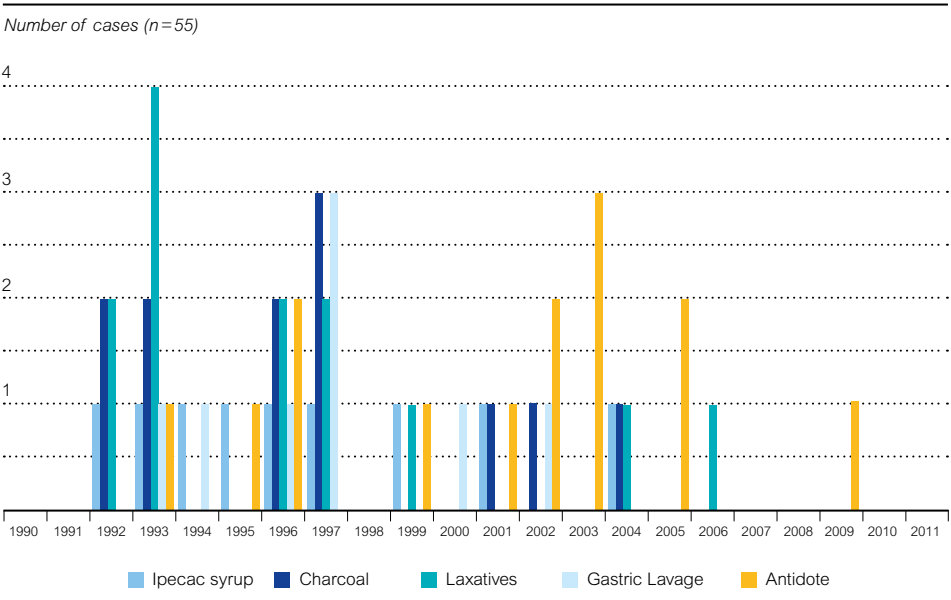

Fig. 7: Comparative representation of the five criteria for the cases considered

In addition to these findings, which could be substantiated by scientific methods, a general change in detoxification therapy has become obvious. Today, a symptomatic therapy is given priority, and removal of the poison has assumed a secondary position. The administration of ipecac syrup, activated charcoal and laxatives as well as gastric lavage have become less important and are found to rather belong to the field of secondary detoxification. In the majority of cases, such therapies are reasonably applied only within the first hour after ingestion of the poison, if not having become obsolete altogether. Presently, the most important therapeutic step in detoxification is characterized by repeated administration of activated charcoal. Nevertheless, also this therapy has not remained undisputed.

The secondary review has demonstrated which research activities and studies can be performed on the basis of the existing data.

It has shown that the case report database can be used as a supporting educational instrument and a sensor, and that it may constitute a valuable component for research by means of linking it with scientific studies.

In particular, the user group of students and teachers can take advantage of the case report database as an e-learning medium to teach and learn also from individual cases. It is a meaningful supplement for teaching and in addition, may support evidence and substantiate studies with evidence-based therapeutic recommendations. The “Case Report Database” research and development project is a contribution to a learning and training system preferentially based on the World Wide Web as a source, which is referred to as e-learning.

2 Selected toxicological problems

2.1 Poisoning by inhalation

Poisoning by inhalation refers to manifestations caused by an uptake of solid, liquid or gaseous chemical toxic agents through the airways into the lungs. Due to the large absorption surface of the lungs, large respiratory volumes and the relatively low alveolar diffusion barrier between the alveoles and the vascular system, the organ provides most favourable conditions for toxic substances to enter the body. The rate at which a substance is absorbed into the body by the inhalation route will depend on the physicochemical properties and the nature of the toxic agent involved.

Pathophysiology

For an understanding of the pathophysiological mechanisms with regard to the toxic damage resulting from inhalation, the different toxic agents are presented in a systematic way.

2.1.1 Aspiration

The direct penetration of solid or liquid toxic agents into the lower airways is referred to as (pulmonary) aspiration. During aspiration, the toxic agents pass the epiglottis and enter the lower respiratory tract. Due to their solid nature, form and diameter, foreign bodies will soon reach a limit of penetration because of the tapered shape of the bronchial system. Once in place, they may well develop a check-valve mechanism resulting in pulmonary hyperinflation.

Liquid substances may, depending on their nature and physicochemical properties, penetrate deeper into the bronchial branches. For dusts, particles and aerosols, the depth of penetration is limited by their physical dimensions and behaviour. Among these, only particles with diameters in the nanometre range (≤ 100 nm) may, similar to small-molecule gases, easily penetrate into the alveolar region. This may also be the case with certain liquids such as paraffins or kerosene. Due to their physicochemical properties like very low viscosity, low surface tension and low vapour pressure, also these liquids are capable of reaching the alveolar region, although with a considerable delay (several hours).

2.1.2 Foreign bodies

The majority of foreign bodies that are swallowed will reach the stomach, posing a gastrointestinal problem in this respect. Experience has shown that even in young children, foreign bodies up to a size of a 2 × 2 Lego brick (approx. 20 × 20 mm) will not lead to direct gastrointestinal obstruction. Toys are tested in this respect according to the Toys Safety

Fig. 8: Risk of aspiration of dangerous lamp oil

Directive[3]. Quite rarely, and mostly in children, swallowed foreign bodies may enter even the lower airways. Young children from one to four years of age were found to be the group most frequently affected. The objects aspirated most frequently by young children are foods such as nuts and bits of raw carrots, and in older children, toys, needles and pins. The right lung is affected somewhat more frequently than the left one.

2.1.3 Particles

Particles and dusts

All over the world, particles and dusts are natural components of the breathing air, with their concentrations depending on the varying environmental conditions. Definitions of particles (particulate matter) and their sizes vary to a great extent, and different disciplines have looked at them in quite different ways so far. By consensus, particles tend to be solid and often are of mineral origin. Their shape tends to be polygonal or roundish, while that of dusts may well be amorphous and fibrous.

Dusts may for example also consist of pollen, which is of purely organic nature. The physical states of dusts may well vary. This also applies to house dust which, depending on the conditions prevailing in a home, may reflect the situation of almost its entire interior including materials, inhabitants, microorganisms, parasites and toxic substances. From the toxicological angle, house dust has a very far-reaching "memory". This means that in the case of modern pesticides such as the synthetic pyrethroids, an exposure to pollutants can be measured even after several years. An indoor deposit important for human exposure is found on the lower back of radiators. First signs of house dust allergy are observed at the beginning of the heating period in the autumn because at that time, large amounts of house dust together with additional summer dust are released from the radiators due to the convection generated.

In a traditional sense, dusts are mostly understood as being of mineral origin (e.g. when it comes to pneumoconiosis), such as coal dust in coal worker's disease (silicosis as an occupational disease), abrasive dusts in metal workers or fibre dusts in asbestos workers (asbestosis as an occupational disease). In the field of occupational medicine, there is an increase of interest in biogenic dusts (proteins, microorganisms), e.g. in farming, the farmer's lung or pigeon breeder's lung being forms of occupational disease referred to as extrinsic allergic alveolitis.

Today, science is making great efforts to differentiate, more clearly than in the past, between the terms of "particles" and "dusts", in order to obtain better results, also with regard to therapy and prognosis. Many people live in arid regions (e.g. desert areas such as the Sahel zone with its mineral dusts), tropical or subtropical regions (with their mineral and biogenic dusts). Due to the prevailing natural conditions, it is impossible in these regions to protect humans from exposure to particles. In addition, there has been an increase in pollution by particles of anthropogenic origin such as domestic fires, industry and transport. Probably, motor vehicles including vessels and aircraft are the main generators of pollution by particles and dusts in the industrialised world. In Germany alone, more and more tyre abrasion is generated, in addition to brake abrasion and motor vehicle emissions because the performance (and thus the acceleration and braking capacity) of cars, motorcycles and motor trucks is on the increase. This applies in particular to electric vehicles because of an unfavourable ratio of acceleration capacity to vehicle weight.

3 *Directive 2009/48/EC of the European Parliament and of the Council of 18 June 2009 on the safety of toys*

Nanoparticles

It is quite difficult to develop an appropriate working definition of nanoparticles which would be suitable, on principle, to describe a group of particles with defined risk characteristics. Nanoparticles contained in fine particles and, especially, in ultrafine particles have become the subject of multiple toxicological studies. Due to the special geometry and surface properties of nanoparticles, the availability of their surface atoms per particle in relation to the volume is assumed to increase exponentially with decreasing diameters, thus producing a special type of toxicity. Humans have been aware of this fact for ages and have made use of it in almost all grinding processes. Everybody knows that the flavour developed by finely ground spices or coffee is by several classes finer than that of the coarse corn or bean. On principle, humans are exposed to natural nanoparticles on a very large scale, e.g. due to geography-related mineral dusts (arid regions, erosion on mountains, general weathering processes etc.), emissions from transport (exhaust gases, brake/tyre abrasion) and industry (combustion processes), volcanic eruptions, forest and bush fires etc. Even seawater aerosol on beaches was found to contain natural nanoparticles due to salt condensation, formed on the basis of waves and depending on the wind. Obviously, ultrafine particles may also form in the aerosol of sprays (see p. 26, Waterproofing spray syndrome) and in many other processes not yet sufficiently examined so far. Even processes like the burning of tea lights, peeling of oranges, baking of cake, toasting of bread, ironing, burning-down of fireworks etc. are associated with an excessive release of nanoparticles. It has to be evaluated on a scientific basis to what extent such processes, that lead to a plausible pulmonary uptake, are of importance for human health in toxicological terms. There have been numerous research initiatives to elucidate this issue. However, the majority of these deal with artificially produced nanoparticles rather than those from known sources of exposure such as cement-producing and cement-processing industry (cement works and building industry/handicraft, respectively).

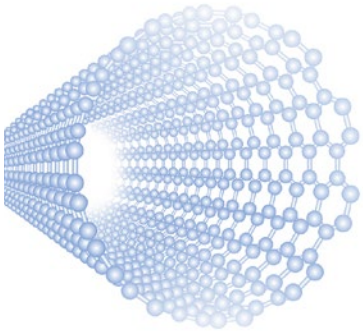

Fig. 9: Nanotube

Pulmonary aspiration of powder

A special form of particle inhalation posing a potentially severe health risk is powder aspiration in infants. Baby powder is no longer recommended for use in the paediatric field. It mostly consists of talc preparations, and some types, of finely ground maize starch flour. In rare cases, but almost always due to a special accident scenario, baby powder may penetrate deep into the lower airways. A typical scenario may occur when the baby is lying on the diaper changing table or an appropriate mat. A powder bottle accidentally opening widely above the baby's open mouth may lead to aspiration of large amounts of powder. Typically, this will be characterized by severe coughing attacks, dyspnoea, stridor and cyanosis. In very rare cases, even respiratory and circulatory arrest may occur. Often, manifestations will disappear almost completely after several minutes. This may be followed by a deceitful asymptomatic interval lasting for up to 24 hours. Health effects developing afterwards may include life-threatening obstruction with atelectasis, severe pneumonia and chronic lung damage.

Fig. 10: Surfactants in liquid detergents

2.1.4 Liquid toxic agents

Pulmonary aspiration of gastric contents

Pulmonary aspiration of gastric contents is the most frequent type of liquid aspiration. On principle, gastric contents will mostly consist of a mixture of liquid, solid and semi-solid substances. The problem consists in the share of highly irritant or caustic components in the gastric acid. Aspiration of gastric contents may lead to diffuse damage to the upper and lower airways, obstruction in the bronchial system and secondary infection resulting in pneumonia.

The effects of pure liquids after aspiration will depend on their physicochemical properties such as pH (acidic, alkaline), water solubility, oil/water coefficient, viscosity, vapour pressure etc. Experience gained especially from human cases of poisoning has shown that after penetrating into the upper lung areas, liquids with a high vapour pressure such as petrol, hexane, alcohols etc., will evaporate very quickly on the mucosal surface. They have an irritant effect on the bronchial mucosa. Nevertheless, they will very rarely cause haematoptysis, as formerly often described, and are mostly exhaled quickly and without sequelae.

Surfactants

More recent experience from cases of poisoning in humans, particularly in children, have shown that liquid solutions of detergents, household cleaners containing surfactants or other types of surfactants, when ingested in small amounts, will not lead to aspiration associated with dyspnoea, pneumonia or lung damage, as formerly assumed. Extensive evaluation of cases has demonstrated liquid surfactants to pose a very low aspiration risk. Problems have been observed only in cases affecting elderly people: Due to arteriosclerosis, severe chronic illness and dementia, their senses of taste and smell may be strongly reduced and swallowing reflexes impaired. As a result, they may well be able to ingest considerable amounts (i.e. more than 100 mL) of cleaners containing surfactants and disinfectants. Ingestion of such quantities will, as a rule, cause vomiting and severe aspiration, which may result in life-threatening health damage and death. In contrast, children's reflexes are so excellent that they will ingest only very small amounts, if any.

Special liquid hydrocarbons posing a risk of aspiration

A particular risk of aspiration toxicity is posed by hydrocarbons such as liquid paraffin (chain lengths of C8 – C16) and kerosene. Due to three physical properties (very low viscosity, very low interfacial and surface tension, very low water solubility), these hydrocarbons may readily "undercreep" the closed epiglottis during the normal swallowing process (physiological swallowing) of small amounts. Little pockets on the larynx, referred to as pyriform sinuses, that normally take up small amounts of liquids and ensure that liquids are prevented from entering the trachea may even promote this process of "undercreeping" by taking up such dangerous hydrocarbons during the swallowing process. Consequently, the dangerous hydrocarbons may continuously pass into the lungs even through the closed epiglottis in the sense of a creeping or spreading process, and not only by droplet aspiration through the open epiglottis.

Once the liquid has penetrated into the larynx, the three physicochemical properties mentioned above will promote further spreading over the lungs. During this process, in particular due to the interface and surface tension, the liquid film will eventually become a monomolecular and therefore, surface-active film, which may spread throughout the lungs and thus, may also reach the alveolar region. The cardinal sign is an immediately occurring and often persistent cough. In addition, vomiting will also develop, frequently with a certain delay. In the onward course, dyspnoea, accelerated respiration, strong thoracic retractions and cyanosis will be observed and, in affected children, sometimes also clouding of consciousness. Within one hour, there will be marked changes in the white blood count, which have frequently been misinterpreted as pneumonia.

Chemical pneumonia will develop in a comparatively high percentage of cases (10 – 23 %), in cases with an initial appearance of signs, even in 25 – 50 %. Specific pulmonary changes can generally be observed within twelve hours after the accident (shadowing, hyperinflation, air-fluid levels, atelectases, colliquative necrosis etc.) and will persist for weeks or even years.

Tissue losses (pneumatoceles), or lung abscesses will often occur, which may considerably reduce the function of the lungs and the lung volume if the tissue does not heal properly. In addition to permanent changes, findings may also include diffuse damage depending on the severity of chemical pneumonia in the deep bronchial system, even as late as 8 to 14 years after the accident and in a high percentage of cases. In cases with a severe course, the patients' condition will deteriorate very rapidly and they will die in spite of artificial respiration. In the concordant opinion of experts, the course of lamp oil aspiration is fateful because even after numerous consultations and assessments by paediatricians, intensive care physicians, physiologists, pharmacists, clinical toxicologists etc., there is still no successful treatment available at present. Therapeutic attempts with artificial lungs, as were performed e.g. in the USA, involve a very high therapeutic risk for infants and young children.

Other liquid hydrocarbons

In many older publications and textbooks, the toxic properties of the group of liquid hydrocarbons have been overestimated and often presented in a rather undifferentiated way. For example, such wrong information included a high vapour pressure (high volatility) to represent the primary toxic property. It was stated that a "toxic" gaseous phase was formed. Pulmonary aspiration of liquid hydrocarbons was presented and interpreted as "chemical inhalation".

According to numerous evaluations of cases of poisoning by inhalation in humans, highly volatile hydrocarbons such as petrol, alcohol and other volatile solvents are aspirated, however, they will evaporate very quickly in the airways

and subsequently exhaled without causing any noticeable symptoms. The liquid components may have a directly irritant effect on the mucosal membranes and, in very rare cases, lead to cough with blood-stained expectoration. In cases where liquids of this type have penetrated deeply into the lungs, there will in fact be a realistic chance for these to become exhaled without a development of risky obstructions or adhesions of the airways, as observed in the case of paraffins or kerosene.

2.1.5 Gaseous toxic agents

Pure gases have small molecules and may be deeply inhaled into the lungs as a mixture with the breathing air. In the alveolar region, gases will mostly diffuse very quickly into the capillaries along a diffusion gradient and are distributed with the blood, depending on their concentration. Gases of toxicological relevance are generally referred to as irritant gases. They also play a certain role in fire gases. The group of irritant gases includes acrolein, ammonia, hydrochloric acid aerosols, isocyanates, sulfur dioxide, formaldehyde, nitrous gases, and phosgene, among others. With regard to their effects, irritant gases are distinguished between those with immediate effect and those whose effects will become apparent after a latency period. Irritant gases with immediate effect include e.g. aerosols and reaction products of acids. On principle, irritant effects occur directly on the mucous membranes of the upper airways. Depending on the concentration, the nasopharyngeal area will be affected immediately. In contact with the moisture of the bronchial mucosa, ammonia will form ammonium hydroxide, hydrochloric acid fumes will condense and formaldehyde will form formic acid. Sulfur dioxide, sulfuric acid, acetic acid and other organic acids will directly irritate the mucosal membranes. Nitrous gases and ozone are poorly soluble in water. Therefore, they will penetrate deeply into the airways and reach the alveolar region with a latency period. This may result in pulmonary oedema developing with a considerable time lag.

2.1.6 Aerosols

Aerosols are mixtures of solid or liquid particles and gases. Their behaviour will always depend on the particles and the carrier gases. An aerosol is a dynamic system which is subject to permanent changes. Due to meteorological influences, the human body is permanently exposed to aerosols. Depending on the weather conditions, these aerosols may have a high

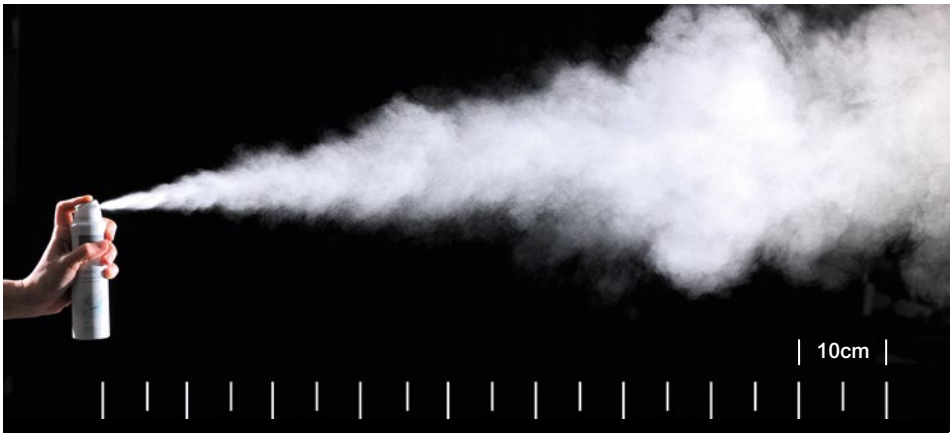

Fig. 11: Spray mist from deodorant

moisture content (water e.g. in fog), or a high content of mineral particles (dust, e.g. desert dust).

Smog

The word, smog, is a compound derived from "smoke" and "fog". In toxicological terms, the share of pollutants in smog is of interest. Smog refers to air pollution in concentrations mostly capable of impairing visibility in large cities. In most cases, it occurs under special meteorological conditions (e.g. thermal inversions) associated with a lack of wind. Smog formation is also promoted by valley or basin topography. Smog may also occur in rural areas due to intensive wood burning and unfavourable topography. In December 1952, the city of London was affected by a disastrous smog episode (The Great Smog) that claimed the lives of up to 12 000 inhabitants. In December 1962, also Germany (the Ruhr region) experienced a severe smog situation with more than 150 deaths. Especially the health of elderly people and children will be affected by smog weather conditions. The exposure to a mixture of soot, sulfur dioxide, dust, ozone, fog and increasing concentrations of nitrous gases may lead to strong irritation of the airways and eyes as well as cardiovascular problems. There has been a marked decrease in air pollution from industry, domestic fires and power plants. However, that from motor vehicle transport has been on the increase. Today, metropolitan smog consists of fine particulates, ozone and nitrogen oxides. The emission of such toxic agents can only be reduced by effectively influencing emissions from motor traffic. Appropriate measures (e.g. the legal requirement of catalytic converter technology) can lead to a decrease in CO and NOx emission. However, from the angle of health assessment, the sum of particle emission from transport and existing particulate matter in the air, in addition to general climate warming under the relatively dry metropolitan climate conditions have to be taken into account.

Fig. 12: Nano waterproofing spray

Waterproofing spray syndrome

Again and again, there have been series of cases where waterproofing sprays, wet blockers or leather care sprays caused poisoning by inhalation associated with sometimes severe health damage (the most recent series occurred in Germany in 2006). A few hours after the "Magic Nano" spray had been introduced into the market these products had to be removed from the shop shelves throughout Germany. The pattern of manifestations including cough, dyspnoea, cyanosis and lung oedema resembled the case series which occurred after the use of several waterproofing sprays in 1982/83 in Germany and in 2002 in Switzerland and the Netherlands. Extensive research into the formulation of nanosprays revealed a great similarity of the chemical spectrum of the relevant components with that of waterproofing sprays. However, it was found that no nanoparticles were contained in the products.

The results of experimental studies on inhalation exposure to Magic Nano sprays have provided plausible explanations for the cases of sometimes severe pulmonary health impairment: Most probably, semi-volatile fluorosilanes

originating from the aerosol plume could penetrate into deep lung areas and thus, the alveolar region as a result of carrier effects involving respirable solid particles. Within a short period of time, the direct – but only temporary – impairment of the surfactant function led to the development of massive pulmonary disturbances including pulmonary oedema. This condition receded spontaneously within two or three hours.

Smoke inhalation

The composition of the smoke produced in fires is mostly very complex. It depends on the material burning, on air supply (i.e. availability of oxygen), and the fire temperature. In addition to carbon dioxide, fire smoke will almost always contain large quantities of carbon monoxide (CO) due to mostly incomplete combustion, and frequently also gaseous hydrogen cyanide (HCN), also known as hydrocyanic acid or prussic acid. In toxicological terms, carbon monoxide and hydrogen cyanide are referred to as the "toxic twins" because both gases have a direct influence on the oxygen function in the body. CO will block oxygen transport, HCN will cause inhibition of oxygen utilization within the respiratory chain. Detailed examinations of fatal cases demonstrated CO and HCN to have strongly additive or possibly even supra-additive effects. These effects are mostly intensified by a lack of oxygen. Smoke consists of a mixture of gaseous, liquid, relatively large solid particles or smut (soot) and in addition, fine and ultrafine particles (nanoparticles). The major component of smoke is formed by aerosols, which will condense also in the bronchial system. Fire fatalities are predominantly to be attributed to smoke inhalation injuries, with the majority of cases caused by carbon monoxide poisoning. In the 1996 Düsseldorf airport fire, 16 out of 17 deaths were due to carbon monoxide poisoning.

2.1.7 Regulation of dangerous paraffin-containing lamp oils and grill lighter fluids

As reported in previous annual reports, paraffin-containing lamp oils and grill lighter fluids had sadly gained notoriety over years due to a number of tragic accidents. Since 1992, the Poisoning and Product Documentation Centre had advocated an improved safety for young children in the sense of regulatory toxicology both among the scientific and expert community and by means of reports to the responsible ministries. Nevertheless, there was only slow progress on the national and EU levels until the problem of health risk could be sufficiently solved. The preliminary final point of legislation that has been achieved in 2014 is an EU Regulation[4] aiming at a complete substitution of or ban on dangerous paraffin-containing lamp oils and grill lighter fluids in the consumer sector.

The regulatory process that lasted for about two decades, as well as the important facts, findings and regulatory steps are explained below.

4 *Commission Regulation (EU) No. 276/2010 of 31 March 2010 amending Regulation (EC) No. 1907/2006 of the European Parliament and of the Council on the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) as regards Annex XVII (dichloromethane, lamp oils and grill lighter fluids and organostannic compounds)*

2.1.8 Risk identification

The cause of health impairments due to liquid petroleum distillates and paraffins was difficult to identify. First sporadic evidence of damage to children's lungs had been provided in 1970 and following years by sparse descriptions of individual cases at the European Association of Poisons Centres and Clinical Toxicologists (EAPCCT). Initially, it was impossible to establish a plausible relationship between these cases because there was no systematic documentation of cases of poisoning available.

In addition, data from standardised animal experiments were flawed. Data from manufacturers' and distributors' spreadsheets were inconsistent. Knowledge on the pathophysiology of liquid aspiration was insufficient. In addition, scientific findings of cases of lipoid or oil pneumonia suggested health impairment in the lungs only to occur in cases where considerable quantities of the toxic agents would enter the lungs.

The problem was that again and again, the parents of the children affected were blamed for such accidents by attributing the incidents to "neglected duty of supervision" instead of the dangerous substance properties of the lamp oils and grill lighter fluids. Retrospectively, it is very difficult to assess why the risk involved for children had not been identified earlier. Certainly, essential reasons consisted in the lack of an appropriate monitoring of the poisoning situation and in the fact that cases of poisoning or, euphemistically, adverse effects of consumer products, did not meet with sufficient attention from the scientific community and the public in the 1970s.

The most important basis for the identification of chemical risks to human health has been established by the German Chemicals Act, which since 1982 has provided a systematic framework for the evaluation of old and new substances. Since 1990, the Cases of Poisoning reported by Physicians under § 16e ChemG and the findings made by the German poison information centres have been compiled at the National Centre for Documentation and Assessment of Poisonings. This has resulted in a permanent generation of scientific data which can explain the relationships between findings in humans, existing data from animal experiments, data sheets and the damage to health observed.

2.1.9 Risk identification problems

Identification of a risk

In Germany, statistically confirmed indications of a special risk for young children from lamp oil ingestion were for the first time brought forward in 1991 by the Berlin poison emergency centre (Beratungsstelle für Vergiftungserscheinungen und Embryonaltoxikologie). At that time, this poison information centre was the biggest one in Germany, with the majority (75 %) of enquiries handled referring to children. Between 1970 and 1990, the number of enquiries and cases treated, respectively, relating to lamp oil ingestion increased from 11 to about 200 per year. The group affected most frequently consisted of children between one and three years of age. One child died from the sequelae of accidental lamp oil ingestion. This issue pointing to a new and most serious risk for young children was given high priority in the work of the National Committee for Diagnosis and Treatment of Poisonings. As a result, regular and systematic analyses of cases of poisoning due to lamp oils and later on, also including grill lighter fluids based on petroleum distillates and paraffins, were performed by the Centre for Recording of Cases of Poisoning at the former Federal Health Office.

The national research project on the recording of cases of poisoning and evaluation (Erfassung der Vergiftungsfälle und Auswertungen – EVA) at the poisoning information and treatment centres in the Federal Republic of Germany

Date	Event
1989	Rapid increase in the use of ornamental lamps using coloured and scented lamp oils in the existing Länder of the Federal Republic of Germany and after reunification, also in the new federal Länder.
1990	Identification of the problem by the National Committee for the diagnosis and treatment of cases of poisoning, start of risk communication
1992	Compulsory use of child-resistant closures for ornamental oil lamp refills
1994	Compulsory inclusion of a warning notice in the labelling of ornamental oil lamp refills
1996	New risk phrase R 65 introduced on the EU level for substances posing an aspiration risk such as lamp oils
1996	Report by the National Centre for Documentation and Assessment of Poisonings on the situation of lamp oil accidents in Germany submitted to EU for the first time
1997	Due to the health risk involved, ban on the placing on the market of coloured and scented lamp oils labelled with R 65 in packaging units of a capacity of up to 15 litres, by EU Directive 97/64/EG of 10 November 1997.
2000	Implementation of EU Directive 97/64/EC of 10 November 1997 in all EU Member States: Ban on the placing on the market of coloured and scented lamp oils labelled with R 65 in packaging units of a capacity of up to 15 litres by 1 July 2000
2000	BfR-ESPED post-marketing study on dangerous lamp oils to record numbers of cases and identify health risks posed by alternative products
2002	European Standard EN 14059: Decorative oil lamps - Safety requirements and test methods
2006	Second report by the National Centre for Documentation and Assessment of Poisonings on the situation of lamp oil accidents in Germany submitted to EU
2010	Commission Regulation (EU) No. 276/2010 of 31 March 2010 amending Regulation (EC) No. 1907/2006 of the European Parliament and of the Council on the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) as regards Annex XVII: Companies placing on the market for the first time lamp oils and grill lighter fluids labelled with R 65 or H 304, are obliged to annually submit data on alternatives to such dangerous substances. Lamp oils and grill lighter fluids labelled with R 65 or H 304 intended for supply to the general public must be packaged in black opaque containers not exceeding a volume of 1 litre. The containers must be visibly, legibly and indelibly labelled with the new risk phrases/hazard statements.
2014	The European Chemicals Agency (ECHA) is requested to prepare, by 1 June 2014, a dossier with a view to completely ban dangerous lamp oils and grill lighter fluids

Table 2: Regulatory measures of toxicological nature in relation to lamp oil and grill lighter fluids

that was launched in 1991 laid the foundation for regular evaluation of cases of poisoning from low-viscosity hydrocarbons in Germany. In 1994, it was possible to conduct a first differentiated assessment of the health risk posed by low-viscosity lamp oils and grill lighter fluids based on petroleum distillates and paraffins in Germany. Regular enquiries among the German poison information centres supplied annual figures describing the risk for young children. The EU-wide partial ban on coloured and scented lamp oils in 2000 was followed by an increasing number of alternative products being placed on the marked, which were examined in the context of a post-marketing study. The corresponding joint study by BfR and the

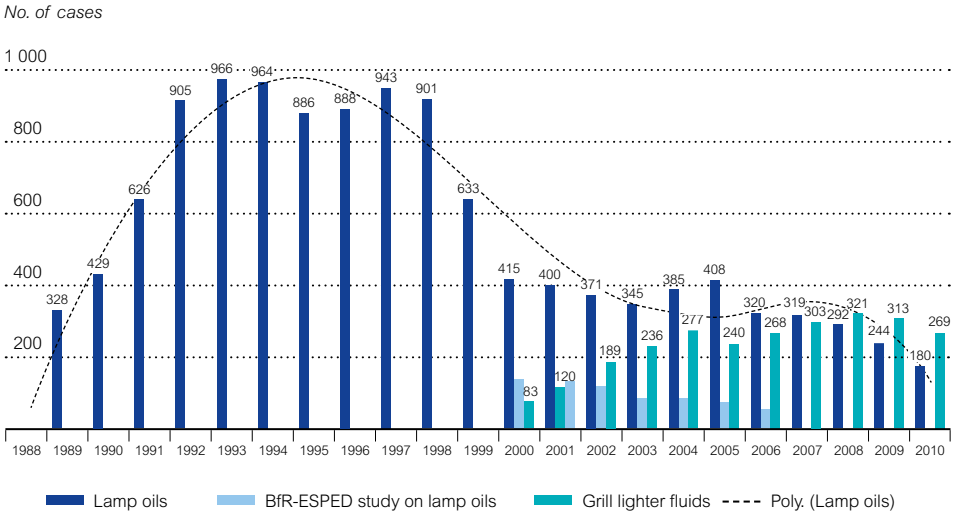

Fig. 13: Cases of poisoning from paraffinic lamp oils and grill lighter fluids

surveillance unit for rare paediatric diseases in Germany (Erhebungseinheit für seltene pädiatrische Erkrankungen in Deutschland – ESPED) meant a prospective recording of cases of lamp oil poisoning in German paediatric hospitals in the sense of an overall survey in the period from 1 March 2000 to 31 December 2006. Almost all paediatric hospitals in Germany were asked to participate in the study. It was intended to record all cases of lamp oil ingestion hospitalized in Germany and include them in the study. In addition to data on exposure and clinical aspects, the study concentrated on the identification of the incriminated products. No special health risk could be identified for the alternative products after intensive enquiries had been conducted by the German poison information centres.

Another risk arising in addition to that posed by liquid petroleum distillates and paraffins formerly used in ornamental lamps was that involved in grill lighter fluids, which had been gaining in popularity. The respective development is clearly demonstrated in Fig. 13. A clear mitigation of the risk for young children could be achieved by additional regulatory measures of toxicological nature (see Table 2, p. 29).

Dose-effect relationship

One of the major problems in assessing the relationship between paraffins and the health risk involved consisted in the supposedly non-existing dose-effect relationship. As a matter of fact, the assessment of the relationship in the case of liquid petroleum distillates and paraffins posing an aspiration risk has been complicated by the dose-effect principle, which is based on the fundamental concept of toxicology (Paracelsus: “The dose makes the poison”).

The realisation was new that already small quantities such as those ingested by sucking on the wick of an oil lamp may cause pneumonia. In toxicological studies in animals, no such effects became evident.

The relationship characterized by the fact that even very small quantities may lead to life-threatening manifestations was eventually derived from the five very well documented cases with fatal outcomes. It was observed that the ingestion of very low quantities of lamp oil caused severe coughing, followed by severe breathing difficulty and, after a deceitful asymptomatic interval, most severe dyspnoea and cyanosis in some cases. All five cases of death in Germany were analysed in detail regarding their entire courses.

Important information was obtained from the third fatality, an infant aged 16 months, who had ingested a plausibly very small amount of lamp oil. The precise amount ingested could not be quantified in an objective way. The infant died about 16 hours later from severe lung failure, in spite of therapeutic efforts. Supply of pure oxygen in mechanical ventilation with PEEP had remained ineffective. Post-mortem findings included all signs of respiratory distress syndrome (RDS), which is not discussed in detail in the present publication. Analyses of representative lung tissue samples of the infant were performed at the Federal Institute for Materials Research and Testing (BAM), using cryogenic gas chromatography coupled to AAS. As a result, it was estimated that probably, a quantity of less than 800 mg of lamp oil aspirated into the lungs had caused complete lung failure.

In contrast to other toxic liquids, the creep capability of liquid petroleum distillates and paraffins posing a risk of aspiration is of particular importance. Once low amounts have penetrated the larynx due to the special physicochemical properties of the liquid, an active toxic process will take place which in the worst case may result in complete lung failure.

Test persons who absorbed low amounts of liquid petroleum distillates and paraffins with their tongues reported to have immediately perceived a spreading process in the oral cavity: The spreading process resulted in single coughs experienced already after a shortperiod (10 to 30 seconds). Not least, the detailed documentation and assessment of the fatal cases helped provide evidence of the relationships. In toxicological terms, the liquid petroleum distillates and paraffins posing an aspiration risk are characterized by a non-linear dose-effect relationship which, however, cannot be directly visualized by a dose-effect graph based on oral dosage.

A sustainable EU-wide regulation of liquid petroleum distillates and paraffins posing an aspiration risk will be completed shortly. Regulation (EU) No. 276/2010 has provided for appropriate prohibitive measures regarding lamp oils and grill lighter fluids becoming effective from 1 June 2014.

Alternative fuels and child-proof lamps have already been developed. In view of the decreasing number of accidents recorded in Germany and based on reports from other European countries stating that aspiration accidents due to liquid hydrocarbons do no longer play a significant role, it can be concluded that a considerable and probably sustainable risk minimization has been brought about by the activities of the BfR Poisoning and Product Documentation Centre.

3 Case reports on current topics

3.1 Aerotoxic syndrome

Based on 35 case reports, the aerotoxic syndrome has been discussed at BfR in the 2011 – 2013 period. On principle, opinions on indoor air hygiene, which also includes indoor air quality in aircraft cabins, are prepared by the indoor air hygiene commission (Innenraumlufthygienekommission – IRK) at the Federal Environment Agency.

The health impairment experienced in aircraft cabins has almost always been associated with unusual smells (smell events) where the odour perceived has been described as “wet dog”, “sweaty socks” or “sweet oily smell”. A study by the UK-based Cranfield University has estimated that oil fumes or other unusual smells have been reported for one in 2000 flights. Actually, this is not an entirely new problem: There have been reports about it already since the 1950ies, however, with increasing frequency over recent years.

The media have repeatedly presented such smell events to cause health complaints often referred to as aerotoxic syndrome. The symptoms mentioned most frequently include drowsiness, vertigo, headache, respiratory tract irritation and paraesthesias such as formication or numbness. These symptoms associated with aerotoxic syndrome are rather general and unspecific and thus difficult to distinguish from those of other illnesses. This is why the term of aerotoxic syndrome has not been officially acknowledged as a disease. Nevertheless, it will be used in the text below for reasons of a better understanding.

Many reports have attributed the development of the symptoms described to a short-term or permanent contamination of breathing air with fumes from engine oil. Since the 1960s, compressed air has been drawn through the engines into the cabin (“bleed air” system) in all common types of passenger aircraft. This is why, according to the German Federal Aviation Office (Luftfahrt-Bundesamt – LBA), there is a possibility of oil droplets leaking from seals which become pyrolyzed and then, may enter the fresh air supplied into the cabin. During such thermal decomposition of jet engine oil, numerous substances may be released including carbon monoxide, carbon dioxide and tricresyl phosphate isomers, but also numerous volatile organic compounds. Some of the products formed have an unpleasant smell or may cause mild irritation at higher concentrations.

The health conditions described have often been attributed to tricresyl phosphate (TCP) as the main cause. In aircraft turbine engine oils (and several other types of oil), this substance

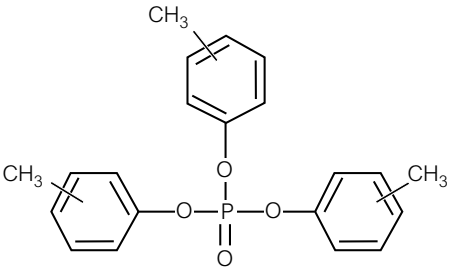

Fig. 14: Structural formula of tricresyl phosphate

is used as an anti-wear additive at concentrations of about 3 %. From the chemical aspect, TCP is the common name for mixtures of ten different isomers. Of these, meta- and para-isomers are significant in quantitative terms. In contrast, the ortho-tricresyl phosphate compounds (o-TCP) considered to be neurotoxic are contained in aircraft turbine engine oils in concentrations as low as about 0.01 %.

Tricresyl phosphates found inside aircraft may also originate from hydraulic oils. The same applies to the structurally related phenyl and butyl phosphates, which have also been detected in aircraft. The latter are also used in flame retardants.

The neurotoxic effects assumed to occur in the context of the aerotoxic syndrome are based on historical reports about mass poisoning from oils containing tricresyl phosphate which at that time still contained high concentrations of o-TCP. The reports referred to incidents when adulterated oil had been sold as cooking oil after World War II in Germany and in 1959, in Morocco. The toxic substance, o-TCP, was also used as an adulterant for Jamaica Ginger, a product that had become very popular to bypass U.S. prohibition laws. However, the incidents of mass poisoning mentioned had always been caused by oral ingestion of very large amounts of tricresyl phosphate. In contrast, the inhalation toxicity of this nonvolatile substance has been considered to be relatively low.

Apart from the neurotoxic component, the symptoms diagnosed in these cases of mass poisoning did not coincide with those described for the aerotoxic syndrome. In the cases of mass poisoning described, the main symptoms observed were cyanosis, feeling of cold, cold sweat or incontinence, in addition to long-term neurotoxicological effects. In contrast, typical disturbances associated with the aerotoxic syndrome such as irritation of the respiratory tract and eyes, headache and dizziness have not been mentioned in the historical reports. Another condition also described in this context and referred to as organophosphorus ester-induced delayed neuropathy (OPIDN) is an extremely rare neurological disease which only occurs after severe organophosphate poisoning (e.g. after attempted suicide). The latency period after exposure is one to five weeks.

Taking into account the amounts ingested in the historical cases of mass poisoning, the route of exposure (in particular, the oral route for oily solutions), the absolutely different concentrations of o-TCP and the diverging symptoms, it has not been plausible in toxicological terms why TCP has regularly served to provide an explanation of the symptoms described for the aerotoxic syndrome. Simple estimates have demonstrated that even inhalation of particularly high o-TCP concentrations detected in aircraft could only result in intake levels that would be lower by several logs than those reported for the cases of oral poisoning.

Air measurements and clinical results

The air in the aircraft cabin is subject to a very high exchange rate. However, a complete separation of gaseous contaminants by means of filters is impossible. The cabin air in aircraft is regulated by a number of national and international rules. The concentrations of pollutants detected are almost always below the levels found in other environments such as the passenger compartments of motor vehicles. Several measurements could confirm a coincidence of odour perception and oil components in the breathing air. However, the concentrations detected were so low that any resulting health impairment appeared to be improbable. In addition to TCP, other phosphoric esters were found such as phenyl and butyl phosphates, which are used e.g. in hydraulic oils and flame retardants.

In numerous studies, air samples from environments both with and without smell events were analysed for the different TCP isomers. In fact,

TCP concentrations above the detection limit were found in single samples. However, all values measured were in the range of a few nanograms or micrograms, i.e. by several logs below the U.S. limit value for occupational exposure to o-TCP of 100 µg/m3. This permissible exposure limit value (PEL) by the Occupational Safety and Health Administration (OSHA) is to serve as a reference in this context in the absence of a valid German/European limit value.

In a large-scale study commissioned by the UK Government, the cabin air quality was tested in different phases of altogether 100 flights. The five types of aircraft examined also included models which in the past had attracted negative attention due to particularly frequent reports of smell events and aerotoxic syndrome. During flights, crew members had again and again, but sporadically, reported smells of oil. However, no significant increase could be found in the concentration of contaminants measured, including TCP and carbon monoxide.

The Institute for Prevention and Occupational Medicine of the German Social Accident Insurance (Institut für Prävention und Arbeitsmedizin der Deutschen Gesetzlichen Unfallversicherung – IPA) performed comprehensive measurements of the exposure of airline crews to tricresyl phosphate and other substances after (oil) smell events[5].

Metabolites of o-TCP could not be detected in any of the more than 300 urine samples, and one sample only was found to contain m- and p-TCP metabolites exceeding the detection limit. Instead, elevated levels of some other aryl and alkyl phosphate metabolites were detected in flying staff members.

Presumably, these were to be attributed to exposure to hydraulic fluids and flame retardants.

Other causes

The odours perceived can in part be explained to have been caused by fumes from meals or from burnt food remnants in the galley ovens, body perspiration, odours from toilets and several other sources.

There are also other possible causes for the health impairments described, and some of these are clearly more compatible with the symptoms experienced, such as elevated levels of carbon monoxide, hyperventilation or insufficient oxygen supply due to technical malfunctions in fresh air supply or pressure compensation. However, carbon monoxide as an assumed cause of symptoms is contradicted by the fact that so far, no source could be identified from which relevant quantities of carbon monoxide could have been released. Also, none of the numerous studies found breathing air concentrations or blood levels that would have been high enough to produce symptoms of the degree of severity described.

Although other compounds such as aromatic amines (e.g. ß-naphthylamine) and volatile organic compounds (VOC) could frequently be detected in the breathing air samples examined, the concentrations detected in the analyses were never of toxicological concern.

This is why in addition to a lack of oxygen or exposure to other possible toxic chemicals, also other occupational factors have to be considered that may frequently lead to unspecific health impairment similar to the symptoms described for the aerotoxic syndrome. These include, among others, jetlag, unfavourable working hours, noise, varying pressure conditions, turbulences and dehydration. This is also suggested by the fact that frequently, only single members of a crew have perceived such smell events or experienced health impairment in the

5 *Schindler, B.K. et al. (2013) Occupational exposure of air crews to tricresyl phosphate isomers and organophosphate flame retardants after fume events. Arch Toxicol 87 (4): 645–648. doi: 10.1007/s00204-012-0978-0. Epub 2012 Nov 21.*

wake of such events. The unspecific character of the symptoms experienced without any measurable exposure recalls other indoor-associated health conditions such as the sick building syndrome and MCS (multiple chemical sensitivity).

Cases reported

An increasing number of cases has recently also been reported to the BfR poisoning database. In these cases, the symptoms experienced during flights were attributed to the aerotoxic syndrome.

An example of such an event with two persons affected (Cases 1 and 2 in Table 3) is described in the case report which follows. The other 33 cases reported to BfR so far (Table 3) showed a mild symptomatology, often including headache, vertigo and respiratory tract irritation. Analysis for TCP, if performed, could not detect the substance in any of the cases reported. Also other possible causes such as elevated carbon monoxide levels could not be confirmed in any of the samples tested.

So far, the BfR has not received any case report mentioning health impairment among passengers. This corresponds to the reports of numerous other studies and has raised the question why irrespective of chronic exposure, the persons reporting health impairment after acute events were crew members without exception. In addition to a higher number of flying hours, an elevated stress level and special work areas such as those near certain sources of odour (e.g. galley ovens), also the aspect of a considerably increased sensitivity to the issue should not be ignored.

Case report

During an approach to landing on a winter evening, two pilots had perceived an unusual smell they described as “sweetish, like that of burnt electrical parts“. According to an interim report by the German Aircraft Accident Investigation Bureau, they developed dizziness, nausea and numbness of extremities shortly afterwards. In the report, the co-pilot (Table 3, Case 1) declared that he had not been able to land the aircraft in spite of having donned the oxygen mask. The pilot (Table 3, Case 2), who felt slightly better than his colleague, was reported to have managed the landing only with considerable effort. According to the co-pilot, the pungent smell was still clearly noticeable in the cockpit after landing. After landing and still aboard the aircraft, the pilot filled in the air accident investigation form. Afterwards, he and the co-pilot were brought to a nearby hospital by paramedics to receive medical attention.

Manifestations/course

During transport to the hospital the pilots were again provided additional oxygen. The arterial oxygen saturation measured in the ambulance was at that time 99 % in both pilots. Their Glasgow coma scale score was the maximum, i.e. 15. According to the medical reports available to BfR, examinations of the co-pilot performed at the hospital did not result in any abnormal findings except an elevated creatine kinase level. Both pilots stated to have had experienced general symptoms and dizziness during landing which, however, rapidly receded during oxygen supply.

Comments

The press reported that the pilots had experienced severe impairment of consciousness during landing. Initially, this description appeared plausible based on the measured blood oxygen levels of about 80 %. However, it was not mentioned that the measuring method

Case	Event		Signs and symptoms			
	Smell	Smoke	Drowsiness / Vertigo	Headache	Nausea	Breathing difficulty
1	x		x		x	
2	x		x			
3	x		x			x
4	x			x		
5	x	x	x	x		x
6	x		x			
7	x			x		x
8	x		x	x		x
9	x		x	x		x
10	x		x			
11	x		x			x
12	x		x			
13	x					
14	x		x			
15	x					
16	x					
17	x					
18		x	x		x	
19		x	x		x	
20		x				
21	x		x	x		
22	x					
23						
24	x					
25	x					
26	x					
27	x			x		
28	x				x	
29	x		x		x	x
30	x		x	x		
31	x		x		x	
32	x		x	x	x	
33	x					
34	x		x			
35	x		x			

Table 3: Summary of all cases reported by physicians in the context of smell events

Case	Signs and symptoms			Laboratory TCP (unknown, neg/pos)	Degree of severity	Causality
	Burning mouth/throat	Paraesthesia	Others			
1		x		unknown	moderate	possible
2		x	Tunnel vision	unknown	minor	possible
3				neg	minor	possible
4		x		unknown	minor	possible
5	x	x	Rhinitis	unknown	minor	possible
6		x		neg	minor	possible
7		x		neg	minor	possible
8		x		neg	minor	possible
9				neg	minor	possible
10	x		Tachycardia	neg	minor	possible
11	x		Tachycardia, eye irritation	unknown	minor	possible
12				unknown	minor	possible
13	x			unknown	minor	possible
14				unknown	minor	possible
15				unknown	none	possible
16				unknown	none	possible
17				unknown	none	possible
18				unknown	minor	possible
19				unknown	minor	possible
20	x			unknown	minor	possible
21	x		Abdom. pain	unknown	minor	possible
22				unknown	minor	possible
23				unknown	none	possible
24				unknown	minor	possible
25				unknown	none	possible
26	x			unknown	minor	possible
27				unknown	minor	possible
28			Eye irritation	unknown	minor	possible
29				unknown	minor	possible
30				unknown	minor	possible
31				unknown	minor	possible
32	x			unknown	minor	possible
33				unknown	none	possible
34	x			unknown	minor	possible
35	x		Eye irritation	unknown	minor	possible

(as of November 2013). Several cases associated with the same event have been listed in one frame.

Fig. 15: Common passenger aircraft

applied was inappropriate for the problem to be investigated and therefore, resulted in misinterpretation. Hence, the oxygen concentration of 99 % measured already in the ambulance appears more realistic. All other laboratory parameters were within normal ranges, except for the creatine kinase level measured in the co-pilot. According to the medical report, the latter could unequivocally be attributed to previous excessive sporting activity. Based on the medical reports available, the description of the pilots' condition as "almost unconscious" that was given in the media reports cannot be confirmed. Probably, it was in part due to the misinterpretation of the initial medical findings.

The first report to the German Aircraft Accident Investigation Bureau initially described a perception of smell followed by indisposition. The pilot was reported to nevertheless have constantly been in control of the situation. Based on this description, the incident was not attached particular importance to. This is why initially, the German Aircraft Accident Investigation Bureau abstained from further investigation. Only two years later, an interim report featuring a clearly more drastic description of the events was published on the Internet. The reasons why the description of the case by the pilots became revised so long after the incident had happened are unknown.

During the technical check of the cockpit by technicians, a smell of de-icing fluid was noticed, according to the aircraft accident report. In contrast, smells of oil or fuel and electrical odours could clearly been excluded, according to the technicians. This is why the investigation report stated de-icing fluid as a probable cause. From a technical point of view, however, it can be assumed that after a flight time of approx. one hour at a speed of more than 800 km/h, any quantities of de-icing agent applied externally should have been removed by the airstream. The toxicologically relevant component of most de-icing fluids is ethylene glycol. This substance is also contained in almost any car radiator coolant fluid. Due to its low vapour pressure and in cool weather conditions as prevailing in winter, ethylene glycol is only semi-volatile. In addition, it is not readily absorbed via the respiratory tract. Symptoms resulting from inhalation would be much more probable in interiors of motor vehicles because malfunctions of car radiators

occur quite frequently and may lead to ethylene glycol vapours from coolant water entering the car interior. However, no such cases have been brought to the knowledge of BfR so far.

Because the incident had happened almost two years ago, records of flight data and communication were no longer available. The technical check performed after the incident did not reveal any technical abnormalities in the aircraft. On the day of the accident, the aircraft had already conducted two flights without any unusual incidents, and it was released to normal duty again the next day.

Evaluation of the case described

There was no toxicological analysis carried out after the event. Nevertheless, based of the technical conditions and the manifestations described, poisoning from tricresyl phosphate or de-icing fluid has been rated as extremely improbable.

Conclusion

From the perspective of BfR, there is currently to indication of any acute risk for aircrews or passengers due to TCP. Fixing of limit values is problematic since tricresyl phosphates are mixtures of isomers with different toxicity levels. In addition, there are merely a few data available based on animal experiments or clinical studies, which refer to the oral route of exposure only and not to inhalation.

The problem has already been addressed by the German Bundestag and the European Commission. In May 2011, the European Aviation Safety Agency (EASA) stated that so far, no serious health hazard could be identified and therefore, there was no urgent need for action. So far, it could not be conclusively elucidated whether certain substances or other causes, if any, could have been responsible for the symptoms described.

As shown in the above case report, a contemporary, comprehensive and technically correct assessment is of absolute importance in such events. The compulsory reporting of cases of poisoning by attending physicians is a very important instrument created by legislation to understand the effects of chemicals in humans. Therefore, particularly physicians working in the field of aviation are asked to comply with the requirement to report cases of suspected poisoning.

3.2 Snapper fillet

First ciguatera outbreak in Germany after consumption of fresh snapper fillets

In early November 2012, 14 cases of poisoning became known in Germany that were attributed to the consumption of snapper fillet, a predatory fish imported from Southeast Asia. Ciguatera poisoning is caused by metabolites of algae resulting from secondary accumulation in this fish species. These substances are referred to as ciguatoxins and can be toxic and even lethal to humans. In addition to the common symptoms of food poisoning (indisposition, vomiting, convulsive abdominal pain and diarrhoea), typical manifestations may include unpleasant sensations such as burning, tingling and pain on contact with cold surfaces that may persist for weeks or even months. A specific phenomenon associated with ciguatera, i.e. ciguatoxin poisoning, is a paradoxical reversal of temperature perception, i.e. cold feels hot and (in some cases) hot feels cold. Patients have described such sensations as extremely disturbing and even triggering anxiety.

The outbreak was first noticed by the Northern Germany Poison Information Centre (PC) located in the city of Göttingen when they received a number of telephone enquiries by patients affected, by physicians and the veterinary authorities of the federal Länder of Schleswig-Holstein, Hamburg and Rhineland-Palatinate. Later, additional cases were reported to have occurred in Lower Saxony and Bavaria. As far as possible, leftovers of fish dishes from the households involved were collected for toxicological analysis. A report via the European Rapid Alert System for Food and Feed (RASFF) and, as early as five days after the first cases of illness had occurred, a nationwide recall were launched by the German Federal Office of Consumer Protection and Food Safety (BVL).

The snapper is a perch-like reef predator indigenous to all subtropical and tropical seas (Indian Ocean, Caribbean, and Pacific Ocean). It feeds predominantly on small fish and other small marine animals (crayfish, shrimps and worms), as well as some plankton species. Some specimens can grow up to a length of one meter, with a weight of up to 20 kg, and may live for as long as 20 years. Particularly in specimens of advanced age, ciguatoxins may accumulate due to long-term feeding on special algae (dinoflagellates), which are harmless to the fish proper.

Case 1

A 59-year old male and his wife consumed about 400 g of home-prepared fresh snapper fillets at about 6 pm. These had been purchased on the day before at a regional supermarket (labelled as red snapper) and stored in a refrigerator until prepared to eat.

About four hours later, both spouses developed nausea, vomiting, watery diarrhoea and severe convulsive abdominal pain. These manifestations were, however, less pronounced in the wife. Due to dyspnoea, imminent unconsciousness and severe gastrointestinal manifestations, and with a tentative diagnosis of foodborne disease, the husband was admitted to a hospital specialised in gastroenterology about three hours after the onset of manifestations.

Manifestations/course

Sonographic examination of the abdomen performed at the hospital revealed dilated intestinal loops with increased peristalsis being in line with the symptomatology of acute gastroenteritis. The patient's pain could not be sufficiently alleviated by morphine administration. Therefore, computed tomography of the abdomen was performed, which analogously revealed dilatation and the presence of fluid in

Fig. 16: Red Snapper

the small and large intestines. Blood parameters and urinalysis were normal except for a mild increase in leukocyte counts found initially. The gastrointestinal manifestations disappeared within a few hours so that the patient could be discharged in a good general condition on the afternoon of the next day.

In the period that followed, the patient's condition was predominantly characterized by neurological manifestations. Numbness of the lips and oral mucosa disappeared after a few days. A considerable nuisance for the patient consisted in itching all over his body, which exacerbated at night on contact with the blanket, as well as a painful hypersensitivity to cold, which was most pronounced on the palms and soles and somewhat less pronounced in the face. In addition, the patient reported to suffer from sleep disturbances.

One week later, the patient presented to a neurological outpatient clinic of a University Hospital for further diagnostic examinations. Electromyography revealed an increase in excitability of muscle membranes as indicated by a series of discharges. Due to the existing allodynia (pain sensitivity) a therapeutic attempt was made by administration of pregabalin (an anticonvulsant medicine whose approved indications include the treatment of neuropathic pain) with a gradual increase of the doses administered. Otherwise, the clinical-neurological status was normal. Itching and hypersensitivity to cold persisted for about three months.

Leftovers of the unprepared fish were submitted to the responsible food control authority for further analysis. The European Reference Laboratory for Marine Biotoxins was able to detect ciguatoxin in the respective sample.

Evaluation of the case described

Based on the information given on the temporal and spatial relationship between exposure and the occurrence of the manifestations observed, and in the absence of other causes, a causal relationship has been rated as confirmed.

Case 2

A 76-year-old male of about 80 kg body weight and about 1.84 m height had bought about 200 g of fresh "red snapper" fillet in a supermarket. The fillet was reported to have originated from a particularly large fish. For supper, he grilled the fish in an oven and consumed about 120 g of it. About four to five hours later, he felt increasingly unwell and weak, suffering from shivers, low blood pressure, cardiac arrhythmia and perioral tingling.

Manifestations/course

Convulsive abdominal pain and diarrhoea persisted for about one week. Weakness, shivers and general malaise persisted for about two weeks, and the cardiovascular manifestations, for about one month. Paraesthesia in the form of tingling was experienced initially in the perioral region, and later on the patient's hands and feet. During the following days, the latter exacerbated to become a "terrible" itching so that at night the patient started scratching the skin on his arms until bloody. Such pronounced paraesthesia persisted for about two weeks. Mild paraesthesia in the finger tips and feet persisted for at least five months after consumption of the fish. The paradoxical cold/hot sensation persisted for about two months. Cold stimuli such as cold winter air in his face, car and other metal door handles on his hands or cold water showers were perceived as extremely hot by the patient. Inappetence persisting for about four weeks resulted in a loss of 4 kg of body weight. The patient developed a pronounced aversion to certain fat-containing foods such as grilled chicken, which he had liked before. He kept to a low-fat light diet on a voluntary basis.

A therapeutic attempt involving the administration of cholestyramine that had been recommended by a physician involved in clinical studies at a University was suspended by the patient on the second day of treatment due to intolerance. He had not contacted any other physician. The patient had informed himself in depth on the internet and in press reports about the ciguatera problem. In an overall assessment, the above case has been classified as moderate according to the poisoning severity score (PSS).

Evaluation of the case described

Based on the information given on the temporal and spatial relationship between exposure and the occurrence of the manifestations observed, and in the absence of other causes, a causal relationship has been rated as probable.

Comments referring to Cases 1 and 2

On the international level, between 50 thousand and 500 thousand cases of ciguatoxin poisoning have been reported every year. In Germany, only single cases of illness after travelling to tropical and subtropical regions had become known before the cases described above. The outbreak observed in November 2012 is the first one that has been associated with the consumption of fish purchased in Germany. The incriminated food consisted of fresh fillets labelled as red snapper that had been bought by an importer from an Indian intermediary. The latter had imported the fish to Germany as (white) snapper (Lutjanidae spp.). Nevertheless, he placed it on the market as red snapper. Red snapper is less often contaminated with ciguatoxin than other snappers. As far as not sold yet, the batch affected was called back immediately after the contamination had become known.

Consumers are not in the position to identify fish containing ciguatoxins. In addition, the level of ciguatoxin contamination cannot be reduced by heating. The risk can be reduced by restricting the placing on the market to subtropical and tropical fish that originate from fishing grounds situated far from coral reefs, or by entirely avoiding the consumption of predatory fish from such waters. Also, the origin of fish products should be completely documented and traceable.

Patients affected by ciguatoxin poisoning will develop nausea, abdominal pain, vomiting, diarrhoea and general physical weakness within a few hours after ingestion. These are unspecific manifestations also observed in other types of foodborne disease. However, they are followed by the neurological sensation disorders typical of ciguatera such as the paradoxical perception of temperatures and other paraesthetic sensations such as tingling and itching that may persist for weeks or even months. Severe cases of illness involving also the cardiovascular system can lead to death. There is no specific therapy. It is recommended to consult a poison information centre for confirmation of the diagnosis.

3.3 Energy-saving lamp (fluorescent lamp)

Energy-saving lamps are compact fluorescent lamps. Their brightness corresponds to that of the commonly used incandescent bulbs, and they were developed as an alternative to the latter. The fluorescent lamp or tube was invented by Edmund Germer in 1926. He made use of the principle of the former mercury vapour lamp emitting blue-green light and achieved a high yield of light in the white visible spectrum by means of a luminescent layer and an increase of pressure inside the lamp.

From about 1938, fluorescent lamps have been produced and used all over the world. A decision to reduce greenhouse gas emission by at least 20 % until 2020 resulted in a ban on incandescent light bulbs, which was finally adopted by the EU Parliament on 17 February 2009.

With the aim of replacing incandescent bulbs, the principle of the fluorescent lamp or tube was consistently miniaturized, the mercury content in the smaller lamps reduced and the efficiency increased. Such enhancement was possible owing to reduced sizes and the use of electronic ballasts. At about the same time as the light bulb ban and the accompanying information of the public, as well as the constantly increasing market share of compatible energy saving lamps, public opposition formed against this process. Such protest had arisen from the realization that a poisonous product containing mercury was to replace the obviously harmless light bulb and be marketed on a legally binding basis.

The case presented was reported from south Germany: A single activated and broken energy-saving lamp was suspected of having caused severe health damage in a child and in addition, the entire house was rendered uninhabitable. Via the media, among other sources, the impression was conveyed that the mercury

from the broken energy-saving lamp had been the cause of the illness suffered by the child.

Case report

In the basement of a house, an energy saving lamp (21 W) broke when a switched-on floor lamp fell over. The father of the inhabitant family picked up the remnants and discarded them. There was no thorough ventilation of the basement room afterwards. In the following night, two children slept in a room adjacent to the basement room where the lamp had broken, while the connecting door between the rooms remained open.

Manifestations and course

During the night, the nine-month-old brother of the patient developed acute spasmodic laryngitis (pseudocroup) and was referred to a hospital by the emergency physician. During the same night, the 5-year-old patient developed a non-itchy rash all over his body (small papulae with a slight erythema/pale wheals surrounded by a reddish area). The rash persisted for about two weeks and receded completely after four weeks. About four days after the energy-saving lamp had become broken the boy developed an increasing hair loss which after four months also included his eyebrows and lashes. Another four months later, the boy developed tremor of his hands, particularly in the morning, and diarrhoea. The conspicuous observations made by the parents during this period included sudden changes of mood and reduced energy. At the time when the energy-saving lamp broke, both parents had been suffering from respiratory tract infection lasting for one to one and a half weeks. This means that all family members had been suffering from a more or less severe and probably virus-related infection of the upper airways.

Both children were repeatedly examined by paediatricians. Because of his hair loss, the five-year-old boy was presented to a specialist in dermatology and allergology where he was diagnosed with alopecia totalis. Against the background of the broken energy-saving lamp, also a poison-related hair damage was considered, perhaps taking into account also the skin rash observed at the same time.

In view of the possible exposure to mercury, stools, urine and blood from both children were tested for mercury. An additional analysis for thallium and lead was carried out because the five-year-old child also presented to a paediatrician specialized in environmental medicine. All measurements in body fluids and other clinical material as well as ambient air measurements did not reveal any elevated mercury levels. Thus, a suspected relevant exposure could be excluded. Likewise, thallium and lead levels were within normal ranges.

In addition to the paediatrician specialized in environmental medicine, the boy was presented to another surgery specialized in environmental health at a university hospital half a year after the incident had happened. Following a thorough assessment of the case and of all available documents, no relationship could be established between the alopecia areata totalis and mercury exposure.

Evaluation of the case described

Based on the available information on the temporal and spatial relationship between exposure and the occurrence of the manifestations observed, and in the absence of other causes, a causal relationship has been rated as improbable.

Comments

Against the background of the (in toxicological terms) incorrect media reports on energy-saving lamps and the risks posed by them, the parents associated the manifestations of their child with the breaking of an energy-saving lamp and described their case in a letter to the editor. This prompted the reaction of an alleged "specialist in mercury poisoning". By means of telediagnosis and without having seen or examined the child, the alleged specialist diagnosed mercury poisoning associated with acrodynia and recommended mercury elimination by means of chelating agents. Eventually, the child was subjected to this treatment although there had been no justified reason to do so.

Based on such intervention, without detailed knowledge of the circumstances, a chain of communication consisting of incorrect and misleading information was triggered. In this way, the precedent case of mercury poisoning due to energy-saving lamps was construed on the basis of a single case of alopecia of unclear origin that occurred in a temporal relationship with the breaking of a working energy-saving lamp and was accompanied by other symptoms experienced by the family, which can plausibly be explained by an unspecific virus infection.

In this brochure, the case has been toxicologically assessed in order to address an important issue in today's world. Not least as a result of media coverage and an exaggeration of risks, the young patient and his family became extremely unsettled and frightened over a long period of time.

Only examination by a specialist at an institute for occupational and environmental medicine could provide the necessary elucidation and technically correct assessment stating that the manifestations observed had not been caused by mercury.

4 Other case reports

4.1 Hand dishwashing detergent

Death after ingestion of a hand dishwashing detergent

A 74-year-old male had ingested a considerable amount of a surfactant-containing hand dishwashing detergent with a suicidal intent. After pulmonary aspiration, the patient developed lung oedema. In spite of intensive medical care, intubation and artificial respiration, the patient died about 16 hours after the ingestion.

Manifestations/course

The patient had ingested about 250 mL of a surfactant-containing hand dishwashing detergent at home with a suicidal intent. This caused repeated vomiting. The emergency physician consulted found rales over the lungs and administered a defoamer. The patient was immediately transported to a hospital where he received intensive medical care. By that time, no symptoms other than moderate tachycardia were observed. Administration of defoamer was continued. About 10 hours after the ingestion, the patient's condition deteriorated considerably, and he developed lung oedema. In spite of intensive medical care including intubation and artificial respiration, the patient died about 16 hours after ingestion.

Evaluation of the case described

Based on the available information on the temporal and spatial relationship between ingestion of the toxic agent and the occurrence of manifestations, and in the absence of other causes, a causal relationship has been rated as probable.

Comments

Surfactants belong to the substances most frequently involved in cases of accidental ingestion, particularly by children. Experience has shown a certain, albeit very low risk of aspiration to arise from spontaneous or induced vomiting after accidental ingestion of surfactants in amounts as commonly ingested by this age group. Although accidents of this type occur quite frequently, severe health damage has been extremely rare. Most cases of this type have a harmless course.

In contrast, most accidents or suicidal actions involving surfactant-containing products among elderly and/or disoriented persons will not have harmless courses. In many of such cases, the patients affected would ingest large quantities of the products, which may lead to pulmonary aspiration and chemical pneumonitis. BfR has received numerous reports on cases of this type. Judging by the reports of cases of poisoning received from physicians, elderly and/or

Fig. 17: Hand dishwashing detergent

disoriented persons have shown to constitute a special risk group. This is why this group, similar to that of children, should be given attention in systematic preventive considerations also in the future. BfR has already drawn attention to this problem in its annual reports of the Cases of Poisoning Reported by Physicians and a number of press releases.

4.2 Drain cleaner

Chemical burns due to oral ingestion of drain cleaner by a young child

When unattended for a short while, a two-year-old child ingested the remaining contents of an almost empty bottle of drain cleaner. Subsequently, the boy developed excessive salivation. He refused the intake of beverages and food and vomited repeatedly. The child was brought to a hospital by emergency ambulance.

Fig. 18: Drain cleaner

Manifestations/course

During the examination, the boy exhibited excessive salivation and retching, but no more vomiting. His lower lip was swollen, his tongue showed a whitish coating and deep chemical burns in the central area. Breath sounds were normal, except for single crackles. The blood count showed lymphocytosis and neutropenia. Values for the other blood parameters examined were found to be normal.

During the next days, endoscopy under sedation was performed repeatedly at the hospital in order to assess the injury and the healing process in the oesophagus, stomach and duodenum. Initial findings included streaky coating in the entire oesophagus. The epiglottis was noticeably swollen. In the region of the cardia, severe inflammation and prominent, partly fibrinous, erosions were seen. The stomach exhibited a large necrotic area in the greater curvature and stained erosions. The medication administered during the one week inpatient treatment included i.v. administration of omeprazol and cefuroxime for antibiotic prophylaxis. In addition, prednisolone was administered by the i.v. route over two days to reduce epiglottis swelling. On the day after the accident, it was possible to carefully reintroduce oral food intake, which was well tolerated by the child. Follow-up examinations performed on the next days showed a discrete improvement of findings. When a follow-up examination was carried out two weeks later, the chemical burns in the stomach were found to have receded. No stricture of the oesophagus was found. However, the lesions in the central and lower regions of the oesophagus were still noticeably coated with fibrin.

Comments

The product involved was a gel-like drain cleaner based on sodium hydroxide. In order to make the contents of such products inaccessible to children, the packaging must be equipped with a special type of closure. It has remained unclear why in this case, the child nevertheless was able to ingest the substance. Due to

their strongly corrosive ingredients, even small amounts of drain cleaner products may lead to severe injuries in the gastrointestinal tract. Because of their strongly alkaline pH, these substances may penetrate deeply into the tissue and lead to necrosis. Liquid preparations will cause particularly severe chemical burns because they are easy to swallow and their special formulation allows them to spread particularly well in the oesophagus and reach the stomach.

During initial examinations, injuries of the nasopharyngeal tract may indicate a possible ingestion, particularly in patients who are unable (e.g. young children) or unwilling (patients after attempted suicide) to provide information. However, oesophageal damage may also occur without visible injuries of the nasopharyngeal region. Other typical signs of an ingestion of corrosive substances are excessive salivation, refusal to eat and vomiting. The first immediate measure to be taken after accidental ingestion of such products consists in drinking of ample amounts of water in order to dilute the corrosive substances ingested. It is not recommended to induce vomiting because this could result in additional damage to the oesophagus due to gastric acid. In the acute phase, swelling due to inflammation may result in breathing difficulty. Medication includes administration of gastric acid inhibitors, glucocorticoids, antibiotics, and other medicinal products. Proton pump inhibitors or H2-receptor antagonists are routinely administered to reduce the risk of reflux oesophagitis. Administration of glucocorticoids is intended to inhibit fibroblast proliferation and thus, reduce the formation of strictures. However, the efficacy of such therapy has been considered as quite disputable. The administration of antibiotics may appear to be meaningful because perforations will increase the risk of a penetration of bacteria into the tissue. However, also without a prophylactic use of antibiotics, a development of bacteriaemia with subsequent septicaemia has been very rare.

Early endoscopy is performed to enable suction of the corrosive liquid and to diagnose necrosis in the oesophagus or stomach. Such necrosis is considered as an indication for surgical intervention. Severe chemical burns may lead to tissue perforation and in the later course, to strictures in the oesophagus. In addition to bougienage (dilatation of the oesophagus), also surgical removal of affected sections may be required.

The death rate from accidental ingestion of corrosive substances is relatively low. However, the incidence of oesophageal carcinoma will increase by about one thousand times, a fact underlining the importance of regular follow-up examinations.

Evaluation of the case described

Based on the information given on the temporal and spatial relationship between exposure and the occurrence of the manifestations observed, and in the absence of other causes, a causal relationship has been rated as probable.

4.3 Peracetic acid

Transport accident involving 15 % peracetic acid in damaged 30 kg original container

During loading operations of agricultural products, an original container of 30 kg of 15 % peracetic acid (PAA) became damaged for unknown reasons. The damage was noticed by the 43-year-old driver when he perceived the pungent odour of the leaking liquid. He removed the container from the car, ventilated the car and cleaned the contaminated surfaces. During these activities, he inhaled the fumes that had formed. Subsequently, the injured man used the car to fulfil other duties assigned to him.

Manifestations/course

The patient consulted a company physician who diagnosed a bronchial irritation. However, neither the manifestations nor any therapy of this condition were described in detail.

Comments

Peroxyacetic acid, also referred to as peracetic acid (chemical name: acetyl hydroxyperoxide) is a colourless liquid having a pungent odour, which chemically is a derivative of acetic acid. The substance, is always present in a chemical equilibrium comprising acetic acid, hydrogen peroxide, acetyl hydroxyperoxide and water. At high concentrations (> 50 to 70 %), peracetic acid will undergo explosive decomposition. This is why sufficient cooling and/or thermal insulation has to be provided during storage and transport. A chemical peracetic acid equilibrium will always involve decomposition at a (more or less) high rate. Since during this process, oxygen becomes liberated, PAA products must never be stored in hermetically sealed containers. Therefore, original containers of PAA products are equipped with gas-permeable closures by manufacturers. Peracetic acid is strongly corrosive to metals. At the same time, PAA is decomposed by steel, copper and brass. To avoid aggressive acid corrosion, PAA working solutions have to be adjusted to a pH of 8 to 10. In addition, PAA is highly reactive with a variety of materials and substances such as

Fig. 19: Handling of dangerous goods

salts of heavy metals, rust, organic substances (oil, fat, cotton, wood, ashes) and synthetic materials (rubber, polystyrene, PVC). In contact with chloride solutions, PAA will form dangerous fumes.

PAA is marketed as a stabilized equilibrium peracetic acid in different concentrations. It is used as an oxidizer, bleaching agent and disinfectant. The bactericidal effect of acetyl hydroxyperoxide has been known since 1902. About ten years later, the substance became known as peracetic acid, in colloquial usage. Owing to its solubility in water and fat, peracetic acid is a strong and rapidly effective disinfectant with a broad spectrum of activity against bacteria, spores, moulds and yeasts, mycobacteria and viruses.

Accidental exposure to PAA of the airways, eyes, skin and mucous membranes may lead to severe health damage. This is why comprehensive protective measures should be complied with both for prevention (wearing of protective clothing and safety goggles, immediate cleaning of surfaces/objects contaminated with PAA, no wearing of jewellery etc.) and in the technical and organizational fields (removal of gases by suction at refilling workplaces, not leaving containers open, avoiding contact with reactive substances etc.). Contaminated clothing must be removed immediately. Skin and eyes that have come into contact with peracetic acid should be rinsed with water without delay.

Peracetic acid should be stored in cool and well ventilated rooms. No other closures than the original ones equipped with pressure-equalizing ports should be used. Direct sunlight should be avoided. Peroxide residues, packages with residual contents as well as contaminated objects are hazardous wastes. Even very small quantities of unused PAA must not be disposed of via the sewer system.

Injured persons having inhaled PAA fumes should be removed from the danger area while observing precautions for self-protection of the helper. Subsequently, artificial respiration and/or an inhalational steroid should be administered. After ingestion of PAA, the patient's mouth should be rinsed with water before giving her/him water to drink.

On the day of the accident, the injured male had loaded the company car with a cryogenic container for the transport of animal sperm and other products to be delivered, which included an intact 30 kg container of 15 % peracetic acid. It has remained unclear how the original canister package became damaged. Likewise, it has been impossible to reconstruct why the car interior (upholstery and carpet) became contaminated with the leaking liquid. During the cleaning operations and the continued use of the car, the patient was unprotected and thus, became exposed to the fumes released.

On principle, at the company affected, tasks of safety technology and occupational medicine are reliably performed by external service providers. Regarding the handling of hazardous substances, corresponding risk assessments had been performed and laid down in writing. In the light of the accident described, the staff were provided with safety data sheets covering the hazardous substances used. When the above transport accident was discussed later on, the company agreed to the necessity of training a member of the staff as a specialist in occupational safety.

Evaluation of the case described

Based on the available information on the temporal and spatial relationship between exposure and the occurrence of the manifestations observed, and in the absence of other causes, a causal relationship has been rated as probable.

4.4 Organophosphate-based insecticide

Accidental ingestion of an organophosphate-based insecticide with fatal outcome in a child

When unattended for a while, a six-year-old boy had drunk a liquid of a colour resembling that of ice tea from an unlabelled PET bottle in a workshop/garage, according to information given by another child. Shortly afterwards, the boy was found lying unconscious on the floor of the premises by his father and an acquaintance. Without delay, they brought the boy to the nearest hospital.

Manifestations/course

On admission to hospital, the boy was unconscious and in an apnoeic and asystolic condition. His pupils were contracted, and his clothes were wet from urine. Blood analysis revealed a marked lactic acidosis (pH 6.88). Cardiac massage and artificial respiration were started immediately. Due to persistent cardiac arrest, the child was repeatedly administered adrenaline and atropine (total dose 10 mg). This was followed by a stabilisation of heart rate and blood pressure. The acidosis detected by blood gas analysis was adjusted by a single short-time infusion of sodium bicarbonate solution. A viscous whitish-orange secretion could be aspirated from the mouth, while it was impossible to aspirate any liquid from the stomach. Because there was a strong suspicion of poisoning, activated charcoal was administered via a gastric tube. The boy's body was cooled by placing cooling pads on his head and inguinal region and in addition, by i.v. administration of cool electrolyte solution. The hypothermic treatment was continued over the next 72 hours.

Fig. 20: Risk of confusion due to storage of dangerous substances in food containers

According to the medical report, an acetone-like smell was observed to emanate from the child. A petrol-like odour was also found to emanate from the bottle delivered in the meanwhile. It was sent to a laboratory for analysis together with a blood sample. Subsequently, transfer of the boy to the intensive care unit of a paediatric hospital was prepared. Since cerebral oedema was suspected, a cranial computed tomography scan was performed before the transfer started. The CT revealed a global cerebral swelling without haemorrhage, which was assumed to have been caused by cerebral hypoxia. For treatment of the cerebral oedema, administration of furosemide, mannitol and dexamethasone was started.

On admission to the paediatric hospital, the boy was still in a comatous condition with unresponsive and contracted pupils. About seven hours after ingestion of the poisonous liquid, first muscular twitching set in, which generalized in the further course. After mevinphos poisoning had been confirmed by analytical detection of a blood level of 13.9 mg/L by the laboratory, a symptomatic treatment with atropine was started. In the next days, mevinphos could no longer be detected in the blood. During the two days after admission, transcranial doppler sonography had not revealed any abnormalities of the systolic and diastolic pressure profile.

However, electroencephalography showed a ubiquitous flat curve, which was only interrupted by high-amplitude phases in the sense of epileptic seizures.

On the fourth day, the boy developed massive diuresis due to central diabetes insipidus. Transcranial doppler sonography revealed an oscillatory flow in the middle cerebral artery, suggesting a lack of blood supply to the brain. Another cranial computed tomography scan confirmed that meanwhile, the generalized cerebral oedema had led to entrapment of nerve pathways. Measurements of the intracranial pressure revealed a maximum value of 157 mmHg. In spite of maximum intensive therapy and symptomatic therapy of the central diabetes insipidus by desmopressin, the boy died a few hours later. To elucidate the causes of death, a forensic investigation was ordered. Post-mortem did not result in any abnormal external findings other than those resulting from the medical measures taken. Examination of the head revealed a marked maceration and swelling of the cerebral tissue with blood-stained liquid in the cerebral chambers. The scull base and foramen magnum appeared to be intact. The vascular circle of the brain base was found to be free from obstructions. The lung tissue was markedly swollen, with ample amounts of yellowish mucous and in part also bloody contents found in the bronchial tubes. Another striking finding was that the urinary bladder of the dead boy was filled to capacity. Based on the massive filling of the urinary bladder and pronounced cerebral swelling, a preliminary medico-legal report assumed a central regulation failure to have been the cause of death.

Comments

Mevinphos is a light yellow liquid used either in a concentrated form or, predominantly, as a 50 % solution in organic solvents such as xylene. It is an organophosphate compound used to control a wide spectrum of insects on vegetables and fruit. It was authorized as a pesticide for the first time in 1957. Due to its very high toxicity and several cases of fatal poisoning, the substance approval was withdrawn in Germany in 1990, in the USA in 1994, and EU-wide, in 2007. The origin of the mevinphos that had been transferred to a beverage bottle and then led to poisoning in the case described above has remained unknown to BfR.

In addition to a higher toxicity, as compared to the majority of other organophosphates, mevinphos will lead to a particularly rapid development of manifestations. If dissolved in organic solvents, mevinphos is absorbed very quickly by the gastric mucosa. Unlike thiophosphoric esters, conversion to an oxygen-containing phosphoric acid compound is not required for this substance to take effect. This is why acetyl cholinesterase inhibition will set in very quickly. Literature data have described cases where death occurred already 10 to 45 minutes after ingestion of the poison. The typical manifestations of poisoning from mevinphos and other organophosphates are causally related to acetyl cholinesterase inhibition. Signs of mild poisoning will include dizziness, nausea, diarrhoea and abdominal cramps. Severe poisoning will lead to lung oedema, respiratory paralysis, convulsions, coma and death. There are hardly any comparable cases of poisoning which could provide reference values with regard to toxic concentrations in humans because mevinphos has been banned for a long time and in many countries. The oral LD50 in the rat is in the range of 3 to 12 mg/kg body weight. After oral exposure, mevinphos is rapidly metabolized by the liver. In addition to primary detoxification and maintenance of vital functions, the treatment of mevinphos poisoning will above all include the administration of atropine as an acetylcholine receptor antagonist. Administration of atropine is carried out in the form of biological titration with increasing doses until a significant reduction of bronchial secretion is found. To maintain the level achieved, atropine administration is subsequently continued by means of infusion.

The efficacy of oximes as acetylcholinesterase reactivators in organophosphate poisoning has generally been disputed. It is important that administration of the antidote is started as early as possible after exposure. Due to ageing processes, and depending on the type of organophosphates, its binding to the remaining serine of the acetylcholinesterase is irreversibly consolidated after a short period of time. Bonds aged in this way can no longer become reactivated by oximes. The two methylester groups contained in mevinphos will cause the substance to age particularly quickly. This is why antidote therapy with oximes is expedient only within a very narrow time window of a few hours.

In the case described above, the diagnosis of organophosphate poisoning was made many hours after ingestion by means of analytical detection of mevinphos in the blood sample. It is questionable whether an earlier diagnosis would have improved the chance of survival for the boy because on arrival to the hospital, he was already found in an apnoeic and asystolic condition and possibly, brain death had already occurred.

The development of cerebral oedema is a dangerous complication of cerebral hypoxia. The increased intracranial pressure will reduce the perfusion of brain vessels, which may lead to ischaemic cerebral damage. If the intracranial pressure comes to exceed systolic blood pressure, cerebral perfusion will cease (brain death). Another possible complication of cerebral oedema consists in entrapments. This condition is associated with parts of the brain being pressed into the cranial fossa and vertebral canal due to the increased pressure. This may lead to interruption of nerve pathways into the brain stem. Also myoclonias, as described in the above case, are among the frequent symptoms of cerebral oedema. The treatment of cerebral oedema will, in addition to administration of osmotic diuretics (mannitol, sorbitol), also include measures such as hypothermia in order to reduce metabolic activity, among other measures. Signs of brain death include missing brain-stem reflexes, flat electroencephalography curves, an oscillatory flow in doppler sonography and development of central diabetes insipidus. This condition is caused by insufficient production of the antidiuretic hormone in the hypothalamus, e.g. due to brain damage. As a result, reabsorption of the water in the collecting tubule is no longer possible, leading to uncontrolled and excessive diuresis.

It has come into question whether in this case, brain death had occurred already immediately after ingestion of the poison and subsequently, merely the vital functions had been maintained for a couple of days due to the symptomatic treatment. Conceivably, the mevinphos poisoning had very soon resulted in respiratory paralysis leading to global hypoxia. Such assumption is also supported by the massive lactic acidosis found on admission to the emergency unit. The cerebral hypoxia could have resulted in an uncontrolled influx of ions and liquid into the brain cells, which eventually led to the development of cytotoxic cerebral oedema. Cerebral swelling has been described several times in cases of poisoning from mevinphos and other organophosphates. Nevertheless, literature has reported only very few cases where cerebral oedema developed and was followed by brain death. The case described above is particularly tragic given that the child became poisoned from an insecticide which actually was banned in Germany 23 years ago and had been stored in an unlabelled beverage bottle. Preliminary proceedings have been opened against the boy's father and the owner of the workshop/garage for neglect of their duty of supervision.

Evaluation of the case described

Based on the information given on the temporal and spatial relationship between exposure and the occurrence of the manifestations observed, and in the absence of other causes, a causal relationship has been rated as confirmed.

4.5 Hydrazine and lithium aluminium hydride

Laboratory accident due to vacuum implosion during experiment with hydrazine and lithium aluminium hydride

During an experiment performed in a chemical research laboratory, a glass vessel imploded that contained hydrazine and lithium aluminium hydride. The 31-year-old patient was brought to the emergency unit of a regional hospital with multiple cut injuries from glass splinters and contamination of the skin on his head and both forearms.

Manifestations/course

On admission to the hospital, the patient was awake and in a normal neurological condition with stable circulation, i.e. generally free from symptoms. After opening of the primary wound dressings, a cut injury of about 1 cm depth was found on the flexural side of the right forearm and another one, of about 0.5 cm length, on the flexural side of the left forearm. Injuries found on the patient's head included a cut of 2 cm length in a tangential position across his right cheek, two cuts of 1.5 cm length on his chin and a lesion of about 0.5 cm on the right side of his neck. The hospital contacted the competent poison centre to obtain information on the toxicity of hydrazine and lithium aluminium hydride. After decontamination by thorough washing and subsequent wound care, the patient was transferred to the intensive care unit for further monitoring. On the next day, the patient was transferred to a normal ward. There were no complications in the further clinical course. Regular follow-up checking of laboratory parameters did not suggest the presence of any hepatic or renal damage. A temporary thrombocytopenia returned to normal values in the further course of treatment. Primary healing of the wounds was noted. After one week of inpatient treatment, the patient was discharged without any symptoms and the wounds being free from irritation. Outpatient follow-up examinations were carried out over the next four weeks. After two weeks of treatment, the patient could return to work.

Comments

Hydrazine is a colourless, oily liquid developing heavy smoke on contact with air. It has exothermic properties, an ammonia-like odour, and it is miscible with water and alcohol. At temperatures above 250 °C, hydrazine will decompose to form nitrogen and ammonia. The decomposition temperature can be lowered by the presence of catalysts such as copper, iron, nickel and molybdenum. Hydrazine-air mixtures may decompose spontaneously at temperatures exceeding 50 °C. In the presence of strong bases, alkali metals, metal catalysts and nitric acid, the reaction behaviour of water-free hydrazine is characterized by explosive and exothermic properties and therefore, highly dangerous. The substance can be detected by means of commercial test tubes or gas warning systems. Due to their high combustion heat, water-free hydrazine and its derivatives are used as rocket fuel and energy source for fuel cells. In the chemical industry, hydrazine is used for a variety of applications, for example as a starting material for the production of plastic materials, dyes and adhesives, for plant protection products and pharmaceuticals as well as for the stabilization of oils, fats and natural rubber (caoutchouc). Furthermore, the substance is used as a corrosion inhibitor and antioxidant. Hydrazine is toxic and is readily and almost completely absorbed through the skin, the digestive and the respiratory tract. About 50 % of the substance is excreted by the renal route. Biotransformation processes lead to the formation of different

Fig. 21: Laboratory chemicals

metabolites whose relevance cannot be reliably assessed in toxicological terms. Hydrazine and its derivatives inhibit various enzyme systems. As a liquid and in the form of vapour, the substance is a strong irritant to the skin and mucous membranes. After absorption of toxic amounts, persons affected will develop central nervous manifestations such as headache, nausea and restlessness. Other manifestations observed will include convulsions, muscular tremor and hyperthermia as well as allergic reactions, hypoglycaemia and functional disorders of the liver and the kidneys. Therapeutic measures that can alleviate the manifestations include thorough rinsing of affected areas and administration of fluids. In severe cases of poisoning, the administration of high doses of pyridoxine (vitamin B6) as an antidote is useful. In addition, monitoring of glucose levels, blood count, hepatic and renal parameters should be performed.

Lithium aluminium hydride is a white odourless powder, which is soluble in ether mixtures and hydrocarbons. Contact with organic substances, halogen-containing solvents such as chloroform, and oxidants such as hydrogen peroxide will involve a risk of explosion. There is a risk of dangerous reactions of this substance with alcohol, ammonia, acids and oxygen. Lithium aluminium hydride is highly flammable. The gases forming on contact with water may ignite spontaneously. In chemistry, lithium aluminium hydride is used as a selective reducing agent. For example, nitro compounds are reduced to primary amines by means of lithium aluminium hydride. In preparative inorganic chemistry, lithium aluminium hydride is used for the laboratory synthesis of numerous hydrides. In toxicology, the local activity of lithium aluminium hydride is of importance because on contact with fats and proteins, it may form soaps and gelatinous alkali albuminates, respectively (colliquative necrosis). After ingestion of the substance, the measures to be given priority will include stabilization of the patient's blood circulation, monitoring of the acid-base balance and prevention of infection, in addition to detoxification (rinsing, administration of fluid) and symptomatic therapy (pain management, protection against a loss of body heat and administration of sedatives).

In a variety of synthesizing procedures, the reaction of hydrazine and lithium aluminium hydride is a basic reaction. When coming into contact with each other, these two chemical substances will readily react and release a great amount of heat. Therefore, they should be added only very slowly and in highly dilute solution. In the case described above, the existing operating instructions, particularly for weighing in of the substances, had not been adequately complied with. For a safe handling of the two substances described above, personal protection measures should be taken. These include the observance of cleanliness at the workplace, wearing of appropriate protective clothing, working under tightly fitting extraction units and compliance with special storage requirements. Also compliance with self-protection principles by helpers is important. Operating instructions informing about dangers and protective measures should be well accessible.

Evaluation of the case described

Based on the available information on the temporal and spatial relationship between exposure and the occurrence of the manifestations observed, and in the absence of other causes, a causal relationship has been rated as probable.

4.6 Carbon monoxide

Suicidal carbon monoxide poisoning due to indoor use of disposable barbecues

The patient was found in an unconscious state in his apartment. He had obviously ignited three disposable barbecues in a confined environment, with suicidal intent. The emergency physician found the patient to be unconscious and without protective reflexes. He provided for intubation and artificial respiration. COHb measurement revealed a level of 50 % (normal range 0.5-1.5 %), so that the emergency physician administered 5 g hydroxocobalamin. Without delay, the patient was transferred to a toxicological intensive care unit for further treatment.

Manifestations/course

On admission to hospital, the patient was still intubated and artificially respirated. His skin was found to have a rosy shade. A Babinski reflex could not be triggered. Otherwise, the patient's neurological status was normal. His extremities were passively flexible. His cardiac sound was found to be pure and free from arrhythmia. Under hyperbaric oxygen therapy and additional volume replacement, the patient's circulation remained stable. No pleural effusions, signs of acute pulmonary congestion, infiltrates or pneumothorax were found by chest X-ray examination performed in a lying position. However, due to rising levels of parameters suggesting infection and suspected aspiration, a calculated antibiotic therapy of amoxicillin and clavulanic acid was started. Echocardiography revealed an incomplete right bundle branch block. Nevertheless, the pumping function and wall movements of the heart remained normal. Due to increasing levels of heart enzymes, the patient was under permanent observation by a cardiologist. In the further course, the cardiac symptoms receded. After gradual discontinuation of artificial respiration, the patient could be extubated on the third day of hospitalization and transferred to the toxicological recovery ward. There, the patient was examined by a psychiatric consultant on the eighth day and transferred to a psychiatric ward on a voluntary basis on the next day. An antidepressant therapy was started by administration of mirtazapine and quetiapine. A neuropsychiatric follow-up examination to be performed after six weeks was recommended in order to exclude carbon monoxide-associated neuropathy.

Comments

Ready-to-use disposable barbecues are relatively small aluminium pans. They are filled with charcoal and equipped with a grill top for cooking meat, sausages or vegetables, serving about two persons. A remarkable property is the relatively long life of embers. However, disposable barbecues must not be used in indoor environments because the incomplete combustion of charcoal will produce carbon monoxide. Other cases of carbon monoxide poisoning due to the use of barbecue grills in indoor environments and other causes have been described in detail in the 2008 annual report on Cases of Poisoning Reported by Physicians.

Carbon monoxide is a colourless, odourless and tasteless gas that escapes sensory perception. Its concentration in indoor air is commonly between 0.1 and 5 ppm. During the use of open fire in indoor environments (charcoal barbecues, log fires in open fireplaces), the carbon monoxide concentration will rapidly increase. Carbon monoxide is also released during the storage of wood pellets. In urban environments, carbon monoxide levels may rise to levels of 200 ppm/0.02 %. In undiluted car exhaust fumes as produced in the absence of a

catalytic converter, carbon monoxide concentrations will reach about 7 000 ppm/0.7 %. Carbon monoxide is released into the atmosphere as a result of volcanic activity as well as of forest and bush fires.

It is a dangerous respiratory poison binding to the iron atom of the red blood pigment, haemoglobin, with a high affinity. The resulting impairment of oxygen transport may lead to suffocation. Manifestations of mild poisoning will include headache, vertigo, vomiting, drowsiness and influenza-like symptoms. Severe poisoning is typically characterized by a cherry-red discoloration of the skin and particularly, the mucous membranes. Higher doses will have a direct toxic effect on the heart and the central nervous system. However, individual susceptibility may vary. At levels of about 150 to 300 ppm/0.015 to 0.03 % and above, the manifestations described will increase in intensity. A carbon monoxide share of more than one per cent in the breathing air will lead to death within one to two minutes. The half-life for elimination of carbon monoxide from the blood is 2 to 6.5 hours. For detection and prevention purposes, portable and stationary warning devices are available that will detect and indicate carbon monoxide concentrations in the range above approx. 50 ppm/0.005 %.

Fig. 22: Beware of carbon monoxide poisoning! Grills should only be used outdoors.

Evaluation of the case described

Based on the available information on the temporal and spatial relationship between exposure and the occurrence of the manifestations observed, and in the absence of other causes, a causal relationship has been rated as confirmed.

4.7 Tattoo, pigment red

Tattoo-associated granulomatous inflammatory reaction with intensive keloid formation

A tattoo and also permanent makeup are produced by targeted insertion of colour pigments into the dermis layer by means of needle puncture. During this procedure, the skin barrier is destroyed, leading to a loss of its protective function, and chemical substances of different types (colorants, solvents, particles) are introduced into the body. Virtually no studies have been carried out so far regarding possible long-term health impairment, metabolization of the numerous chemical substances involved and triggering of allergic reactions. The most frequently observed undesirable consequences of such tattooing may include (severe) allergic reactions and inflammations requiring medical treatment over extended periods of time.

Also tattoo removal may involve problems. Laser treatment is offered frequently, however, there are also procedures using liquids for tattoo removal. As a rule, these are solutions containing 40 % L(+) lactic acid. Similar to the procedure of tattooing, tattoo removal is performed by subcutaneous injection of the removal agent, i.e.

by perforating the epidermis. Advertisements for substances of this kind claim that the colour pigments were repelled in a natural way.
In a risk assessment (BfR opinion No. 033/2011 of 1 August 2011), BfR has concluded that health risks are involved in the use of highly concentrated (40 %) lactic acid. According to the current state of scientific knowledge, irritant effects may occur on contact with the skin and mucosa already at a concentration of 20 % of lactic acid in formulations and on contact with the eyes, already at a concentration of 10 %. This is why tattoo removal should be performed only by means of procedures recognised by medical science and by physicians.

Special caution should be exercised regarding temporary tattoos which are painted on the skin. Such tattoos are not tattoos in the proper sense because the colorant is applied onto the surface of the skin, penetrating only into the epidermis. These temporary tattoos ("temptoos") or henna tattoos are quite popular with children and adolescents and are frequently offered in holiday destinations abroad. Often, henna is used that has been given a darker shade by means of para-phenylendiamine (PPD). Henna, an extract of the henna plant (Lawsonia inermis), has been known for centuries and in many cultures as a means to dye hair and nails and for decorative body painting. PPD is a known contact allergen which can cause allergic reactions. The use of this substance in henna tattoos is banned in Europe. Also henna has not been approved for use as a colorant in cosmetics.

A typical case has been described in the Cases of Poisoning Reported by Physicians 2004 annual report: An 18-year-old female sought medical advice from a physician because she was suffering from reddening and swelling of her skin, particularly in the region of a tattoo she had made ten days earlier in Malta. A problem was seen in an insipient keloid formation, which, however, completely receded after local cortisone administration (ointment) after an extended period of time. Neither the name of the product nor the manufacturer could be identified.

PPD is also known as a hair dye. Persons who have experienced sensitisation to PPD may exhibit allergic reactions to this substance over their entire lifetime. Meanwhile, increasing numbers of cases of contact dermatitis due to henna tattoos have been described.

On 25 September 2012, BfR pointed to this severe risk in the context of a student workshop, which was attended by a total of 118 students. Adverse effects of tattoos such as infection, scars and allergic reactions were discussed by BfR experts, a Berlin tattooist, a specialist in dermatology and a patient suffering from severe allergic side effects (see case report).

Case report

A 57-year old patient who already had several tattoos on his body had a special tattoo applied with magenta colorant in an area of about 20 × 10 cm on his right lower leg. On the next day, he experienced extensive reddening and swelling, hyperthermia, itching and scaling of the skin in this area. After several cortisone preparations had been administered over an extended period of time and outpatient care for about eight months, the patient was eventually admitted to a university hospital specialized in dermatology.

Manifestations/course

The skin with the coloured tattoo on the right lower leg, sized about 20 × 10 cm, was purulently infiltrated, erythematous and exhibited scaly changes, particularly in the lower part. Histological findings revealed a tattoo-associated granulomatous inflammatory reaction with intensive keloid formation with no indication of malignity. Large parts of the tattoo were excised, and the wound was covered with split skin graft transplanted from the upper leg. After

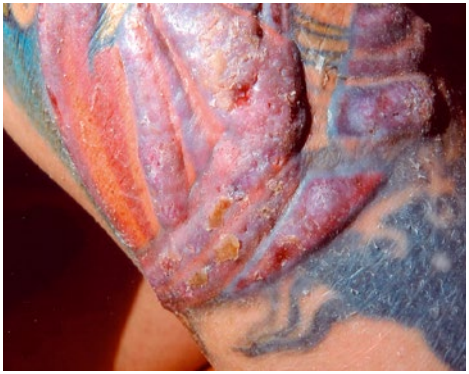

Fig. 23: Tattoo-associated granulomatous inflammatory reaction with intensive keloid formation

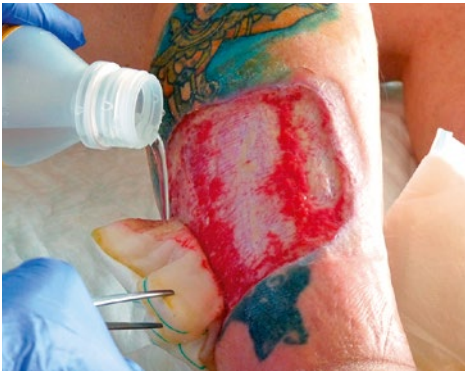

Fig. 24: Large parts of the tattoo were excised

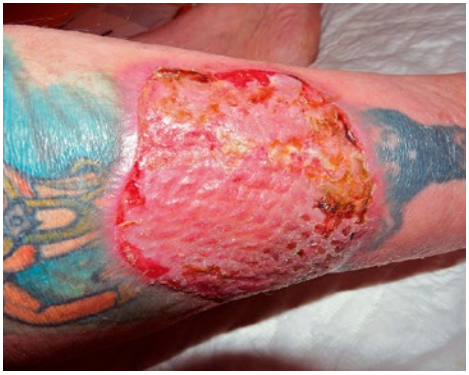

Fig. 25: After split skin graft transplantation

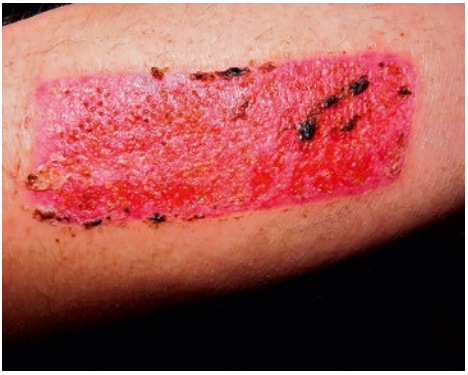

Fig. 26: Donor-site wound on the upper leg after split skin grafting

three weeks of inpatient treatment, the patient was discharged in a stable general condition and with the wound being free from irritation.

Evaluation of the case described

Based on the available information on the temporal and spatial relationship between exposure and the occurrence of the manifestations observed, and in the absence of other causes, a causal relationship has been rated as probable.

Comments

The patient was discharged with a diagnosis of ulcerative allergic contact dermatitis after tattooing with red magenta colorant. Since the patient was not tested for a specific sensitisation, the diagnosis could be established in the sense of a “clinical probability” only. The patient made thorough enquiries with the tattooist in order to identify the ingredients of the ink she had used. However, these resulted only in orienting information on the ingredients instead of a complete formulation. In addition to a pigment red 269, the formulation listed the solvents, tetrahydrofuran and dichloromethane, furthermore titanium dioxide, an undefined extract of North American witch hazel and benzothiazolinone as a preservative. No more detailed information on the formulation (e.g. concentrations) was available, in spite of additional enquiries made by BfR.

It is assumed that most probably, (numerous) other substances are contained in such preparations. Benzothiazolinones such as MCI/MI (methylchloroisothiazolinone/methylisothiazolinone), are known to have a strong sensitizing potential and to cause cross allergic reactions. In epidemiological terms, this group of substances has considerably gained in importance recently with regard to reactions indicating a sensitization. The reasons for this include, among others, the fact that these preservatives are used in many cosmetics, shampoos and meanwhile, also in a great number of dispersion paints. In the context of cases of poisoning reported by physicians, BfR has received reports even of cases of airborne allergic reactions in previously sensitized persons. Thus, strong allergic reactions of the skin were experienced by persons after they had entered a room freshly painted with dispersion paint.

This is why in the case described above, it is questionable whether the allergic contact dermatitis has in fact to be attributed to the red magenta colorant. No tests were performed in this respect.

Tattooing is very problematic because substances are pressed into the skin directly and over extended areas via needle/cannulas operated by means of mechanical tattoo machines (up to 10 000 pricks per minute). This procedure will lead to a destruction of the skin barrier in the region of the tattoo. Particularly if tattoo machines are used, the ink is no longer inserted in the form of very small homogenous droplets but instead, due to the high mechanical energy, in the form of finest components and particles. Because of the enormous spreading of the substances and the great number of pricks, the body's immune system will no longer be able to localize these processes. This is why chemical substances pressed under the skin in an unphysiological way may easily lead to extensive inflammation associated with excessive skin formation. It remains to be seen to what extent such development may result in carcinogenic sequelae at a later age. In a summarizing view, tattooing means an extensive destruction of the epidermis and injection of ink components representing unphysiological substances in the subcutis. Against this background, sufficient safety in terms of health cannot be provided neither by means of a "positive list" of safe substances nor an authorisation procedure for tattoo agents.

4.8 Adhesive flap

Health impairment due to swallowing of an adhesive flap

During a walk, an infant lying in his pram suddenly became ill after having appeared to feel well before. He showed motor unrest, retching, cough and excessive salivation. The parents presented the child to the emergency ward of the nearest hospital.

Manifestations/course

At the hospital, the little patient presented with an acute impairment of his general condition. He continued to be restless while cough and retching persisted. A deterioration of such manifestations was observed when the infant was in a lying position.

The parents reported their child to have played with a pack of paper handkerchiefs and bitten on a piece of paper. Inspection of the throat revealed excess salivation and a marked reddening and swelling of the posterior pharyngeal wall, the palatal arches and the uvula. Deep throat inspection did not result in any indications of the presence of a foreign body. Also X-ray of the chest and soft neck tissues did not provide any explanation for the child's condition. To prepare laryngoscopy, a sedation attempt was made which triggered a strong gag reflex. As a result, a transparent flap of a tissue pack was retched upwards and could be removed easily. When the foreign body had been removed, the

infant was still markedly exhausted, however, his general condition clearly improved. The little patient stayed at the hospital for one night for observation. He could be discharged on the next day in a state of subjective well-being and was referred to outpatient follow-up care.

Comments

The widely used paper handkerchief packs like that involved in the above case are often given to infants and young children as a grasping toy or to divert attention because of the crackling noise they make. Therefore, it makes sense to draw attention to a rare risk by reporting this case. The diagnosis was complicated by the fact that in this case, the adhesive flap was transparent instead of coloured, as seen on some other products showing this closure mechanism. This is why the flap was invisible in the infant's pharyngeal region both for the parents and for the attending paediatricians. Eventually, the flap was only discovered by chance when laryngoscopy was prepared at the hospital.

According to paediatric intensive care experts, adhesive flaps have been involved in aspiration accidents in children much less often than nuts.

With regard to early risk identification, it is recommended to discuss and consider whether such adhesive flaps should be coloured, on principle. Preventively, it is recommended that infants and young children should not be given packs with adhesive flaps for playing.

Evaluation of the case described

Based on the available information on the temporal and spatial relationship between exposure and the occurrence of the manifestations observed, and in the absence of other causes, a causal relationship has been rated as confirmed.

4.9 Food supplement

Health impairment due to consumption of a food supplement

An adult had consumed a food supplement in the form of tablets containing magnesium, calcium and vitamin D3 for an unknown period of time. Due to an acute deterioration of his state of health, the patient was admitted to a hospital.

Manifestation/course

The patient showed weakness in his legs, hyperkalaemia with an initial value of 7.9 mmol/L (reference range: 3.5 to 5.5 mmol/L), forceful vomiting, acute renal failure and intestinal obstruction (ileus). After administration of repeated return flow enemas, three tablets could be discharged two days later. No information was available on the further course.

Comments

All tablets taken by the patient were compared with the tablets discharged as to their size and appearance. According to the information given by the reporting hospital pharmacist, the intestinal obstruction found in the ileocoecal region of the small intestine had been caused by a persisting tablet conglomerate resulting from insufficient or missing dissolution of the tablets ingested. In addition to BfR, also the pharmaceutical company was informed of the case by the hospital dispensary.

Case reports of this kind are submitted by BfR also to the responsible food control authorities of the federal Länder. Possibly, the adverse effects observed in the case described had to be attributed to inadequate preparation regarding the dosage form of the product. This is why this individual case may be of general importance. It has to be assumed that the same manufacturing method is also used for other products so that other products could have been affected as well.

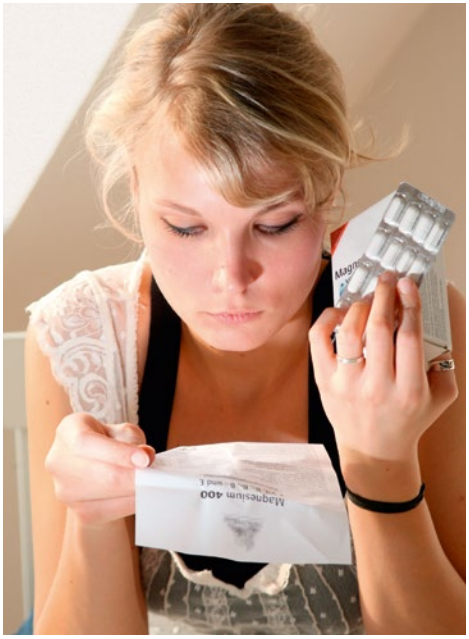

Fig. 27: Food supplement

In legal terms, food supplements have a special position. According to § 1 of the German Ordinance on Food Supplements (Verordnung über Nahrungsergänzungsmittel, NemV), food supplements are foodstuffs. Consequently, they are subject to the relevant provisions of food legislation.

The above case demonstrates the decisive role of the preparation of a food supplement. It is crucial for the efficacy of the product. Not only in the field of food supplements, but also in that of medicinal products, the type and form of preparation constitute an essential part of the technological process of manufacturing.

Food supplements are marketed also in different dosage forms designed for intake in measured small unit quantities. Therefore, the science of dosage forms plays a crucial role also in this field. Today, pharmaceutical technology is one of the most up-to-date pharmaceutical disciplines. It is closely related to the fields of drug safety, the safety of food supplements and also of cosmetics. The number of companies offering food supplements and over-the-counter (OTC) pharmaceuticals has been on the rise. In view of the great variety of preparations, the fast development of technology and the manifold offers found particularly on the Internet, customers and patients will more urgently than ever depend on qualified advice and service by specialist staff.

In recent years, BfR has published numerous opinions and reports on food supplements (e.g. BfR press release No. 34/2012). For these and for more detailed information and presentations on this issue, readers are referred to the BfR website.

Evaluation of the case described

Based on the available information on the temporal and spatial relationship between exposure and the occurrence of the manifestations observed, and in the absence of other causes, a causal relationship has been rated as possible.

4.10 Honey from Turkey

Poisoning due to ingestion of honey from Turkey

A 56-year-old male lost consciousness when driving his car in traffic, and his car came to a stop on the oncoming lane. He was brought to a nearby hospital by emergency ambulance. Later, the patient's brother stated that the patient had eaten two spoonfuls of a wild honey of Turkish origin before the accident happened. A subsequent analysis of the honey by liquid chromatography tandem mass spectrometry (LC-MS/MS) carried out at BfR revealed a concentration of 27 mg/kg grayanotoxin III and by using another semi-quantitative method, concentrations of about 900 mg/kg grayanotoxin I and 116 mg/kg and 304 mg/kg respectively, of two compounds with structures very similar to that of grayanotoxin I.

Manifestations/course

On admission to the emergency ward, the patient exhibited severe bradycardia with a severe drop in blood pressure to 60/30 mmHg. In addition, first-degree AV block was established. The patient was still in a state of clouded consciousness and sweaty. He complained of headache and abdominal pain. Therefore, symptomatic treatment consisting of stabilization by administration of fluid and atropine was followed by a whole-body computed tomography to exclude internal haemorrhage. The patient was monitored at an intensive care unit. On the next day, he could be discharged without symptoms.

Comments

The wild honey of Turkish origin involved in the above case is also referred to as Pontic honey or "mad honey". Such honey is mainly produced in small beekeeping establishments on the Turkish Black Sea coast. The main source of food for the bees kept in this region consists of nectar and pollen from Rhododendron ponticum and related species of the Ericaceae family. These plants are known to contain relatively high levels of grayanotoxins. These are polyhydroxylated cyclic diterpenes. Of the 60 types of grayanotoxins known, types I and III are the most relevant ones in toxicological terms.

Pontic honey is also referred to as "bitter honey". Because of its bitter and slightly irritant taste, it does not normally serve as a food but is used for medical purposes only. The quantity of honey ingested in the above case amounted to about 25 g, i.e. it was in the range of cases of poisoning reported in the past (5 to 30 g). The reasons for using Pontic honey for medical purposes were examined in a Turkish study. An enquiry made among beekeepers from the Black Sea region revealed a great number of customers to consume this type of honey either to alleviate gastrointestinal complaints or to support therapies for the control of diabetes, arthritis and hypertension.

Fig. 28: Pontic Honey

However, the main motive for consuming such honey of Turkish origin has been its reputation to be an aphrodisiac and potency enhancer. These findings have been supported by the fact that according to the respective studies, up to 86 % of the patients affected were males (of an average age of about 55 years.). No information has become available as to the motivation for eating the honey from Turkey in the case described above.

The typical manifestations of grayanotoxin poisoning are similar to those of M-cholinergic syndrome. Mild poisoning will lead to sweating, excessive salivation, nausea, dizziness and blurred vision. Higher grayanotoxin doses may result in hypotension, bradycardia, paraesthesia and disturbances of consciousness. The term of "mad honey" is based on the potential of such honey to trigger hallucinations if relatively high amounts are ingested. The pathomechanism involved is based on a blocking of sodium channels in the cell membrane. Depolarization will lead to hyperexcitability of the nerve cells, which may explain manifestations such as tingling, numbness and other types of paraesthesia. Likewise, due to the permanent polarization, the cardiac muscle cells become subject to a calcium influx which can explain the risk of cardiac arrhythmia.

Arrhythmia, hypotension and bradycardia are potentially life-threatening conditions. Therefore, poisoning from Pontic honey will, in the majority of cases, be treated symptomatically by i.v. administration of atropine and infusion of isotonic saline. As in the case described above, the majority of patients treated as described above will recover within a few hours. In the majority of cases, all manifestations will have receded after 24 hours, except for a mild feeling of weakness. Since treatment by administration of atropine and saline infusion has become available, not a single fatal case of poisoning from Turkish wild honey has been documented in recent times.

To the knowledge of BfR, no systematic studies have been conducted and become known regarding the concentrations of grayanotoxins found in Pontic honey. However, these concentrations and the composition of the individual types of grayanotoxins can be assumed to depend on the regional flora. In addition, they may vary considerably due to a possible blending with other types of honey. This may explain why also persons actually familiar with the use of such honey from Turkey are among the patients affected by poisoning.

As far as known to BfR, there has been no report in international literature which would have established a correlation between quantities of grayanotoxins ingested through honey and the resulting manifestations of poisoning. However, in its opinion No. 043/2010, BfR already reported a case of poisoning where an unknown amount of honey from Turkey with a resulting poison concentration of 43 mg/kg body weight had been ingested under similar circumstances. Also in that case, the patient had developed bradycardia and disturbances of consciousness. Likewise, there have been virtually no animal studies on the problem so far. A less recent study performed in 1971 found LD50 values of 1.28 mg/kg body weight for grayanotoxin I, and of 0.908 mg/kg body weight for grayanotoxin III, after intraperitoneal injection of these toxins. In the case reported above, consumption of about 25 g honey resulted in an uptake of about 0.7 mg grayanotoxin III and 22.5 mg grayanotoxin I.

Only a few cases of poisoning from Pontic honey have been reported from outside Turkey. These were almost exclusively attributed to products originating from Turkey. BfR is unaware of whether such products can be purchased also in Germany. Nevertheless, also physicians practicing in Germany should be familiar with the problem. In cases with corresponding manifestations physicians should consider a possible ingestion of Pontic honey as a cause. At Central European latitudes, rhododendrons

are grown as ornamental plants in relatively small numbers only. Therefore, honey produced in these regions can be assumed not to contain any grayanotoxin concentrations that would be relevant in toxicological terms.

Based on the above case as well as other cases of poisoning reported to BfR, Pontic honey has to be considered as harmful. It is urgently recommended to refrain from consumption of such honey for medical purposes or as a food.

Evaluation of the case described

Based on the information given on the temporal and spatial relationship between exposure and the occurrence of the manifestations observed, and in the absence of other causes, a causal relationship has been rated as probable.

4.11 Hydrogen cyanide from bitter almonds

Health impairment due to hydrogen cyanide due to ingestion of bitter almonds

The female patient had bought a 50 g package of bitter almonds (Prunus dulcis var. amara) at a health food shop which she had mistaken for normal almonds. She ingested the entire contents of the package in the evening from about 6 p.m. Minutes later, the patient collapsed in the entrance to a house. By an ambulance she was brought to the emergency department of a hospital.

Manifestations/course

The patient presented at the hospital in an unconscious state and with a suspected poisoning of unclear cause. Her Glasgow coma scale score was only 3 to 4. Other findings included sufficient spontaneous breathing, moderate protective reflexes and a minor bruise on the patient's knee. Monitoring of the patient was started immediately. Examinations of the heart, computer tomography of the head and sonographic examination of the abdomen resulted in normal findings and did not provide any clue as to a clear diagnosis. Blood gas analysis revealed a pronounced lactic acidosis of 155 mg/dL (reference range: 4.5 to 14.4 mg/dL) under stable cardiovascular conditions. In the further course, the patient slowly regained consciousness. Four hours after admission to the hospital, she was awake and adequately responsive. Her circulation was stable, while lactate levels had markedly decreased. Repeated vomiting of granular pulpy masses was observed. When the patient had become responsive again, she reported her purchase of (bitter) almonds at a health food shop and her consumption of the entire contents of the package. She remembered an initial sensation of heat she had perceived before she collapsed and fainted. The patient recovered, she was, in the further course, found in a stable cardiopulmonary condition and thus, could be discharged soon. Based on the evaluation of the clinical and laboratory findings, the patient had experienced poisoning from hydrogen cyanide acid after ingestion of raw bitter almonds.

Administration of 4-dimethylaminophenol was omitted because of the potential adverse effects of this antidote.

Comments

In rare cases, administration of 4-dimethylaminophenol (even at correct doses) may result in excessive formation of methaemoglobin requiring treatment. Particularly asthmatics may sporadically develop hypersensitivity due to the sodium metabisulfite contained. The effects of 4-dimethylaminophenol in infants and young children have not yet been examined.

In addition to the sweet almonds (Prunus amygdalus var. dulcis) edible in a raw state, there are bitter almonds (Prunus amygdalus var. amara), which are unsuitable for raw consumption. The latter are generally smaller and more pointed than sweet almonds. They have a tart and bitter taste. The typical smell of bitter almond is very

well perceived by most people. However, some individuals are unable to perceive this smell due to their genetic disposition. Bitter almonds contain about 2 to 4 % amygdaline. This is a glycoside from which highly toxic hydrogen cyanide is split during the process of digestion, in the presence of water and the enzyme, emulsin. Cooking of bitter almonds, however, will result in the heat-sensitive hydrogen cyanide to become reduced to harmless levels.

Cyanide ions entering the human body will be tackled by the body's own detoxification system. By means of rhodanide synthetase, a mitochondrial enzyme, the highly toxic cyanide ions are converted into rhodanide (thiocyanate), which is a harmless substance. However, the activity of rhodanide synthetase in the human body is limited due to the limited amount of sulfur available on the intracellular level. This is why only small quantities of cyanide ions can be neutralized by the body. The body is able to metabolize about 30 mg hydrogen cyanide. This is why in cases of mild cyanide poisoning, administration of 4-dimethylaminophenol is not required but instead, administration of sodium thiosulphate is indicated. It will provide the sulfur required for the formation of rhodanide synthetase and is therefore administered as an antidote in cases of hydrogen cyanide poisoning.

Levels of hydrocyanic acid in bitter almonds may reach up to 3 000 mg/kg. In children (depending on their body weight), about five to ten bitter almonds may cause severe health disturbances or even lead to fatal poisoning from hydrocyanic acid. Adults would have to ingest about 50 bitter almonds (approx. 0.2 g hydrocyanic acid) to suffer poisoning from hydrocyanic acid. This was the case in the female patient affected, who had consumed about 50 bitter almonds, corresponding to about 50 g. Meanwhile, bitter almonds are commercially available in small packages (50 g) only. The packages are labelled with a variety of warnings such as "Unsuited to be eaten raw", "Caution, bitter almonds contain hydrocyanic acid, consumption of more than small amounts can lead to death" or "Use only for cooking and baking. Keep out of the reach of children". The lowest lethal dose of hydrocyanic acid for adults has been stated by EFSA (European Food Safety Authority) to be 0.5 – 3.5 mg/kg body weight. In a risk assessment, the UK Committee on Toxicity has recommended that a daily intake of hydrocyanic acid of 0.02 mg/kg body weight should not be exceeded. Likewise, the Committee of Experts on Flavouring Substances of the Council of Europe (2005) has established a temporary maximum daily intake (TMDI) of 0.023 mg/kg body weight.

Amygdaline is not only contained in almonds. This substance is also found in other kernels that are considered as popular snacks and offered on the internet as an alleged remedy: This refers particularly to sweet and bitter apricot kernels. They have also been used in food production for a long time (e.g. persipan). In 2007, in a risk assessment and a press release (07/2007, among others), BfR has pointed out that the consumption of apricot kernels may lead to poisoning and therefore, involves a health risk.

Evaluation of the case described

Based on the available information on the temporal and spatial relationship between exposure and the occurrence of the manifestations observed, and in the absence of other causes, a causal relationship has been rated as probable.

4.12 Atropine and scopolamine

Potentially fatal poisoning due to consumption of coffee poisoned with angel's trumpet

In a household, several persons had been drinking coffee from a coffee machine in the morning hours. Later on, two of these persons developed severe circulatory disorders, which required admission to a hospital. Three other persons complained of a very dry mouth or diarrhoea.

Manifestations/course

The first person affected had had six cups of coffee in the morning. A few hours later, he developed xerostomia associated with thirst and nausea. He also complained of dizziness, severe circulatory problems and hallucinations. Then he lost consciousness and was found by coincidence only after several hours. He was initially admitted to the stroke unit of the local hospital with a tentative diagnosis of cerebral ischaemia. Eventually, anticholinergic syndrome was diagnosed at the hospital. Since the patient's condition improved soon he could be discharged already after one day of inpatient observation.

Fig. 29: Angel's trumpet (Brugmansia suaveolens)

Another person affected had had a cup of coffee during the same morning. She likewise developed a dry mouth, circulatory problems as well as speech and gait disturbances. She was also admitted to the stroke unit of a hospital with a tentative diagnosis of cerebral ischaemia. In the evening of the following day, she could be discharged from inpatient treatment as well.

No information has been submitted on the therapies administered to these two patients.
Three other persons who had also had some coffee from the same coffee machine likewise complained of a dry mouth. One of these developed diarrhoea in addition in the night that followed. However, none of these affected persons sought medical treatment.

Comments

Further enquiries revealed that an extract of angel's trumpet had been used when preparing the coffee, with a criminal intent. In the context of toxicological analysis, atropine and scopolamine could be detected both in the water from the coffee machine and in a urine sample.

The angel's trumpet (Brugmansia suaveolens) is an ornamental plant of up to 5 m height with strikingly large funnel-shaped flowers. All parts of the plant contain the tropane alkaloids, scopolamine (approx. 80 %) and hyoscyamine. Atropine is a racemic mixture of L-hyoscyamine and D-hyoscyamine, which is formed during harvesting and storage. The tropane alkaloids mentioned have identical spectrums of activity, however, with different potencies and specificities. Their action is based on an antagonism among the muscarinic receptors of the parasympathetic nervous system. The anticholinergic activity becomes manifest in the form of visual disturbances with dilated pupils, dry skin, urination disturbances and a dry mouth as reported by all patients affected in this case. In the central nervous system, elevated concentrations of tropane alkaloids will lead to states of agitation, disorientation, convulsive

seizures and hallucinations due to the blocking of acetylcholine receptors. Such manifestations of poisoning may persist for up to two days. In the above case, the central manifestations observed such as disorientation and loss of consciousness initially resulted in the tentative diagnosis of cerebral ischaemia.

Due to its euphoric effects, angel's trumpet is often consumed in the form of infusions or by smoking with abusive intent. For patients suffering from severe anticholinergic symptoms, intensive medical observation is required. Patients developing severe states of agitation and convulsive seizures should be restrained and, if required, treated with diazepam or barbiturates with a short period of action. As an antidote, the acetylcholinesterase inhibitor, physostigmine, is often used. However, bradycardia has to be taken into account as a possible adverse reaction in these cases. Primary detoxification is often achieved by administration of activated charcoal. Due to the dry mucous membranes of mouth and throat, gastric lavage should be performed in exceptional cases only. In cases undergoing timely treatment, poisoning from angel's trumpet has a favourable prognosis.

In the above case, no late sequelae will have to be expected to occur in any of the persons affected. However, if the physician had not been found by chance, the poisoning could have resulted in a potentially fatal situation. For all other affected persons, the poisoning has not been rated as potentially fatal.

Evaluation of the case described

Based on the information given on the temporal and spatial relationship between exposure and the occurrence of the manifestations observed, and in the absence of other causes, a causal relationship has been rated as confirmed.

4.13 Ricin and aconitine

Health disturbance due to suicidal ingestion of castor plant seeds and monkshood

A male ingested 100 castor plant seeds and a root tuber of monkshood (Aconitum napellus) one evening. After having put both ingredients into a blender, he ingested the mixture together with water. He had ordered both the castor plant seeds and the monkshood on the Internet. He was admitted to a local hospital on the same day, suffering from anuria, vomiting and diarrhoea.

Manifestations/course

On admission, the patient stated to have experienced repeated vomiting as early as one hour after ingestion of the poison, which he assumed had resulted in removal from his body of about three quarters of the amount ingested. Due to pronounced exsiccosis, he was administered 3.5 L of fluid for volume replacement. Three days later, he was transferred to the toxicological department of a university hospital.

With persisting anuric renal failure, bloody diarrhoea, exsiccosis and vomiting. After one course of dialysis, the blood levels of substances normally excreted in the urine could be markedly reduced. Subsequently, the patient's spontaneous urine production was sufficient so that repeated dialysis was not required. Regarding the blood count, pathological values were found as follows: Leukocytes 34 550/µL (reference range: 4 000 to 9 000/µL), erythrocytes 6.7 million/µL (reference range: 4.5 to 6.0 million/µL), haemoglobin 21.0 g/dL (reference range: 14 to 18 g/dL), haematocrit 59.0 % (reference range: 40 to 48 %), creatine kinase 1 801 U/L (reference range: < 140 U/L) and C-reactive protein 8.9 g/dL (< 0.5 mg/dL). For testing for ricin and aconitine, samples were submitted to an external laboratory. The patient repeatedly tested positive for Clostridium difficile, also at the toxicological department.

Therefore, administration of metronidazole was started as an antibiotic treatment. In addition, ampicillin therapy was started due to elevated inflammatory parameters and unclear focus of infection. This therapy could be discontinued six days later. Later on, testing for Clostridium difficile was negative, and diarrhoea came to a halt after eight days. On discharge, the patient did not state any gastrointestinal complaints. The patient attended two psychiatric consultations at the hospital. These resulted in a diagnosis of paranoid schizophrenia. Quetiapine medication was initiated, and the patient agreed to be transferred to a psychiatric hospital.

Fig. 30: Palma Christi (Ricinus communis)

Comments

The castor bean plant (Ricinus communis), also referred to as Palma Christi, is cultivated on a large scale mainly in India, Brazil and China where it is used for the production of castor oil. In Germany and other countries of Europe, it is often grown as an ornamental plant. Above all, the seeds of the plant are poisonous. They have a taste similar to that of hazelnuts. Ricin, a toxic protein compound found in the seed coats, is one of the most toxic proteins occurring in nature. It is a water-soluble, lipid-insoluble and heat-sensitive protein. In chemical terms, the protein is a lectin that can specifically bind to cells and cell membranes, respectively, triggering biochemical reactions from this position. It consists of a cell-binding component and a toxicity-mediating component. Cells contaminated with the poison will die. In children, lethal poisoning may already result from ingesting 3 to 5 well-chewed seed beans (one seed bean weighing about 700 mg). Quantities of 10 to 15 well-chewed seeds suffice to kill an adult, corresponding to about 5 µg ricin per kg of body weight. The ricin concentration in the seeds is about 1 to 5 %. In cases of ricin poisoning, manifestations will set in about 2 to 24 hours, in rare cases up to three days after ingestion of the seeds (depending on the degree of mastication/crushing). They will include vomiting, abdominal pain, bloody diarrhoea, convulsions, renal failure, liver damage and collapse and may result in death. Not only the ingestion of seeds but also dermal contact is potentially harmful: Contact with the skin may lead to severe allergies and rashes, particularly in the case of perforated seeds such as used for exotic necklaces. Since the hard seed coat is perforated in these seeds, the toxic substances may have direct contact with the skin. This is why such necklaces must never be used as toys. Also inhalation of castor seed meal may result in allergic manifestations and skin reactions. First aid measures include immediate spitting out of the seeds and drinking of large amounts of fluid. After dermal contact, the skin areas affected should be washed. So far, no antidote has become known. Castor seed meal (fertilizer) and castor oil (laxative) do not contain ricin. Unchewed or poorly chewed seeds are tolerated in higher amounts, in most cases resulting in minor manifestations only. However, it is often difficult to assess (particularly if children are affected) to which degree the seeds have been chewed/crushed when ingested. Therefore, a physician or an emergency service should always be contacted. The degree of severity of manifestations is also determined by the route of exposure (oral toxicity is markedly lower than that on inhalation or injection),

Fig. 31: Monkshood (Aconitum napellus)

the time when vomiting sets in as well as the consistency and a possible pre-treatment of the seeds. Heat treatment will result in an inactivation of ricin. In the above case, the patient benefited from early vomiting of the toxic substances. Analytical detection of ricin is possible by immunological methods, mass spectrometry and bioassay.

The monkshood (Aconitum napellus), also referred to as aconite, wolfsbane, monk's blood, blue rocket or friar's cap, is a plant native to the banks of streams and moist meadows in mountainous regions. It is often grown as an ornamental plant in gardens. It is the most poisonous plant indigenous to Europe. All parts of the plant are toxic, and particularly so, the root tuber and the seeds. All parts of the plant contain toxic diterpene alkaloids, with aconitine being the main alkaloid. The aconitine concentration found in the leaves is 2 %. The highest alkaloid concentration (up to 3 %) is found in the tubers in winter. For an adult, the lethal dose of pure aconitine is as low as about 2 to 6 mg. Consequently, ingestion even of a few grams of fresh vegetal matter will suffice to reach such a dose. Poisoning will become manifest as early as 15 minutes after ingestion of the plant. The poison is rapidly absorbed through the mucous membranes, particularly those of the gastrointestinal tract, but also through the intact skin. First manifestations will include tingling and burning sensations in the mouth and throat, which may be followed by numbness of the tongue, hands and toes. In severe cases of poisoning, the further course will be characterized by agonizing vomiting, colicky diarrhoea, episodes of sweating, respiratory paralysis and cardiac arrest. The toxic effect is based on an increased permeability of irritable membranes for sodium ions, a prolongation of sodium influx during the action potential and a delay of repolarization of sensory and motor nerve terminals. Due to the stimulation of peripheral sensory nerve terminals, various reflexes are induced. High concentrations of acotinine will result in a paralytic effect on the sensory nerve terminals, and in addition, an initial stimulation and subsequent inhibition of the central nervous system. Effects on the heart consist in reflectory bradycardia and a stimulation of secondary and tertiary pacemaker centres resulting in episodes of arrhythmia. Death will result from cardiac arrest caused by ventricular fibrillation or central respiratory paralysis.

Alkaloids are also readily absorbed through the skin. Therefore, manifestations may result even from plucking the plant or touching the flowers e.g. by children playing with them.

Cases of poisoning have frequently occurred due to the tuber being mistaken for celeriac or horseradish roots. The leaves are known to have often caused poisoning when used as a salad green either due to ignorance or because

they were mistaken for parsley. Ingestion or suspected ingestion of any amount of the plant material has to be rated as potentially fatal. Due to a possible rapid onset of dramatic manifestations, persons affected should be transported to a hospital accompanied by an emergency physician. The first measures to be taken should consist in removing remaining parts of the plant from the patient's mouth and ensure the intake of ample amounts of fluid. Recommended therapeutic measures include immediate gastric evacuation by performing gastric lavage. Subsequently, activated charcoal should be administered, and the patient should be monitored at an intensive care unit. In cases of most severe arrhythmia (torsade de pointes), initial administration of magnesium at high doses is recommended, followed by continuous infusion. In cases of bradycardia, administration of atropine is indicated. Currently, no specific antidote is known (for ricin, also cf. case report 4.14).

Evaluation of the case described

Based on the available information on the temporal and spatial relationship between exposure and the occurrence of the manifestations observed, and in the absence of other causes, a causal relationship has been rated as possible.

4.14 Ricin and alcohol

Health disturbance due to suicidal ingestion of castor plant seeds and alcohol

A female with a history of schizophrenia and depression persisting for more than ten years had discontinued her medication regimen and ingested 80 castor beans, which she had crushed in a blender, together with alcohol. She had found this suicidal method on the internet when searching for information on poisonous plants. She then ordered the castor beans from a German trader of gardening supplies on the internet. The seeds were packaged in sachets containing eight beans each and labelled as "Wunderbaum" seeds (German common name for Ricinus communis). On the trader's website, there is a warning because of the toxicity of the seeds, and the recommendation of keeping them away from children. The online trader was unable to give any information on the Ricinus communis subspecies of the seeds offered because they had been purchased from an intermediary. Therefore, it was impossible to establish whether possibly, a variety producing less ricin was involved or the ricin contained in the seeds had already been depleted by heat treatment. On that evening, the female ingested ten times the amount known to her to be a lethal dose. She had decided to use the castor plant because she had read that the poison could not be detected or was difficult to detect. 24 hours later, she was admitted to a hospital with gastrointestinal manifestations (vomiting, abdominal pain and diarrhoea) that had been persisting for almost the same period of time.

Manifestations/course

On admission to hospital, the patient was generally oriented. The findings included an absence of neurological manifestations and stable vital parameters. The patient was found in a general depressive mood. The pathological laboratory

parameters recorded included:
Sodium 133 mmol/L (reference range: 135 to 145 mmol/L), GOT 60 U/L (reference range: 10 to 35 U/L), GPT 136 U/L (reference range: 10 to 35 U/L), gamma GT 61 U/L (reference range: < 39 U/L) and leukocytes 18 700/µL (reference range: 4 000 to 9 000/µL). In the further course, blood-stained stools were observed. Three days after ingestion of the poison, the patient was transferred to the toxicological department of a university hospital. There, the blood parameters listed above were still in pathological ranges. In addition, an increase in creatine kinase to 1 334 U/L (reference range: < 140 U/L) was found. The clinical picture recorded there was merely characterized by abating gastrointestinal manifestations so that the patient could be transferred to a normal ward on the next day. No examination to detect the poison was carried out. A toxicological analysis revealed positivity for metamizole and metoclopramide in urine. Psychiatric consultation resulted in a diagnosis of schizophrenia and depression already known for more than 10 years and mentioned in the patient's history. Follow-up examinations recommended on discharge of the patient included analysis for electrolytes, of renal, hepatic and inflammatory parameters and a blood count. The medication given on discharge included metoclopramide, lorazepam and potassium effervescent tablets to be taken if required, and pantoprazole (40 mg) as a regular oral medication.

Comments

It can be assumed that the castor seeds involved in this case had been pre-treated so that their poison content was considerably reduced or completely destroyed (for ricin, also cf. case report 4.13).

Evaluation of the case described

Based on the available information on the temporal and spatial relationship between exposure and the occurrence of the manifestations observed, and in the absence of other causes, a causal relationship has been rated as possible.

4.15 Hydrogen cyanide from cherry laurel

Health impairment in a goat following ingestion of cherry laurel leaves

A Thuringian Forest Goat had eaten about 1 kg of cherry laurel leaves when unattended for a while. Subsequently, the animal developed gastrointestinal symptoms and apathy. The animal was therefore admitted to a veterinary hospital. No further information has become available as to the type of husbandry and location of the animal.

Manifestations/course

The goat was admitted to hospital as late as two days afterwards. The animal presented increasingly apathetic and refused food and water. When arriving at the hospital, it was found to be already somnolent. Clinical examination revealed acral coldness, pale conjunctivae and a pronounced abdominal breathing. Auscultation revealed highly pronounced moist rales over the lungs. Laboratory findings included severe leukocytosis accompanied by a left shift, mild anaemia, mild thrombocytosis, hyperglycaemia, hypomagnesaemia, a vast increase in urea levels in the serum and an elevated creatine

Fig. 32: Also animals can be at risk of poisoning

kinase level. The animal was initially subjected to symptomatic treatment because the history of an ingestion of cherry laurel leaves was still unknown at that time. The goat died on the day of admission.

On the post-mortem pathoanatomical examination performed, the rumen, reticulum and omasum were found to be filled with large quantities of fibrous matter. The latter consisted of a great amount of poorly masticated leaves, which later could be identified as cherry laurel leaves. In addition, severe acute alveolar lung oedema, mild serofibrinous pleuritis and diffuse catarrhal enteritis were found to be present in the animal.

Comments

The leaves and seeds of the cherry laurel (Prunus laurocerasus) contain cyanogenic glycosides, especially prunasin (1 to 1.5 % prunasin in fresh leaves). In contrast, the fruit pulp of the plant does not contain any appreciable amount of the poison. Cherry laurel, particularly in the form of chewed leaves, is toxic to horses, cattle, goats, sheep, swine, dogs, cats, hares, rabbits, rodents (guinea pigs, hamsters) and birds. Especially in ruminants, the cyanogenic glycosides are split in the rumen by the action of microbial enzymes, resulting in a release of cyanide ions. On contact with body fluids, cyanides will capture a proton, thus being present as undissociated hydrocyanic acid. As a result, the latter is able to penetrate lipid membranes. Cyanide ions will unfold their activity in the cells, binding to the central iron(III) ion in the mitochondrial respiratory chain. They have a binding affinity superior to that of oxygen. Therefore, continued oxygen binding in the blood is inhibited, resulting in a blocking of the respiratory chain. A sensation of “internal asphyxia“, and death after a few minutes will follow. Manifestations of poisoning will include salivation, irritation of the mucous membranes, abdominal pain, nausea, vomiting, gastric and intestinal disturbances, signs of paralysis and respiratory problems. Severe poisoning may result in respiratory paralysis. The lethal dose in cattle is 500 to 1000 g of cherry laurel leaves. Confirmed lethal cases have been recorded in horses as well. An animal that has nibbled on cherry laurel should be encouraged to drink a lot of water. Continued uptake of the poison into the body can be reasonably prevented only within the next 30 to no more than 120 minutes by administration of an emetic, a laxative or gastric lavage. In any case, a veterinarian should be contacted immediately. After emergency treatment and reliable diagnosis, administration of an antidote such as sodium nitrite, sodium thiosulphate or 4-dimethylaminophenol can be considered.

Cherry laurel is also poisonous to humans, particularly children. Already chewing of a few seeds will result in an amount of hydrogen cyanide being released that may cause first symptoms in a child. These may include nausea, vomiting dizziness and stomach pain. Fortunately, the plant and its leaves have an unpleasant taste so that ingestion of major amounts by children or adults is rather improbable. However, cherry laurel is not only known for its toxic effect but has also been used for therapeutic purposes. In homeopathy, the plant is used for the treatment of cough, hoarseness and cardiac insufficiency. Thus, the oil of the cherry laurel has an antispasmodic effect and is also used for the treatment of asthma and whooping cough.

Evaluation of the case described

Based on the available information on the temporal and spatial relationship between exposure and the occurrence of the manifestations observed, and in the absence of other causes, a causal relationship has been rated as probable.

5 Results of reports by physicians

5.1 Evaluation of reports

During the period from 1 August 1990, i.e. the beginning of the compulsory reporting, to 31 December 2013, altogether 77 663 reports on cases of health impairment, poisoning or suspected cases of poisoning were received by BfR. During the 2011 to 2013 reporting period, 13 225 case reports received by BfR. Of these, 11 952 reports were submitted by the Berufsgenossenschaften (BGs, i.e. the professional insurance bodies) and 1 273, by physicians working in hospitals, medical practitioners and other medical institutions (cf. Fig. 33).

The share of reports submitted by hospitals and medical practitioners has remained low. Evaluations by the poison information centres have shown that the number of health impairments occurring after absorption of or contact with chemical products, household chemicals, plant protection and pest control products and all other reportable product groups has remained high and does not correspond to the number of reports received by BfR.

5.2 Cases of poisoning reported in the 2011 – 2013 period

5.2.1 Origin

As in the past, the majority of reports were submitted by the Berufsgenossenschaften (BGs). In 2011, these accounted for 89 %, in 2012, for as much as 92 %, and in 2013, for 90 % of the total number of cases reported. The number of reports received by BfR from hospitals and medical practitioners accounted for 11 % in 2011, 8 % in 2012 and 10 % in 2013.

5.2.2 Spectrum of cases reported

In the reporting period, cases involving chemical/physicochemical agents ranked first among the reports submitted by the Berufsgenossenschaften (cf. Fig. 34). Among the reports submitted by hospitals and medical practitioners, the majority of health impairments had been caused by products of daily use and chemical/physicochemical agents as well as primary substances. The category of primary substances is intended to comprise case reports where BfR was only reported the chemical substance name. Often, only the toxicologically relevant ingredient is reported although a certain product was involved. Nevertheless, the name of the product and its intended use are not mentioned in the report.

About 8 to 10 % of the cases reported referred to health impairments caused by medicinal products, although these are not subject to compulsory reporting under § 16e ChemG.

For a detailed list in tabular form of toxic agents reported to BfR since the beginning of compulsory reporting in 1990, see Annex (Chapter 6.3). The causative agents have been combined to form product application groups (assignment of toxic agents according to their intended use).

5.2.3 Circumstances of poisoning

More than 98 % of the case reports submitted by the Berufsgenossenschaften referred to accidents. Only 0.2 % of cases of health impairment had occurred after the common use of the substance or product involved.

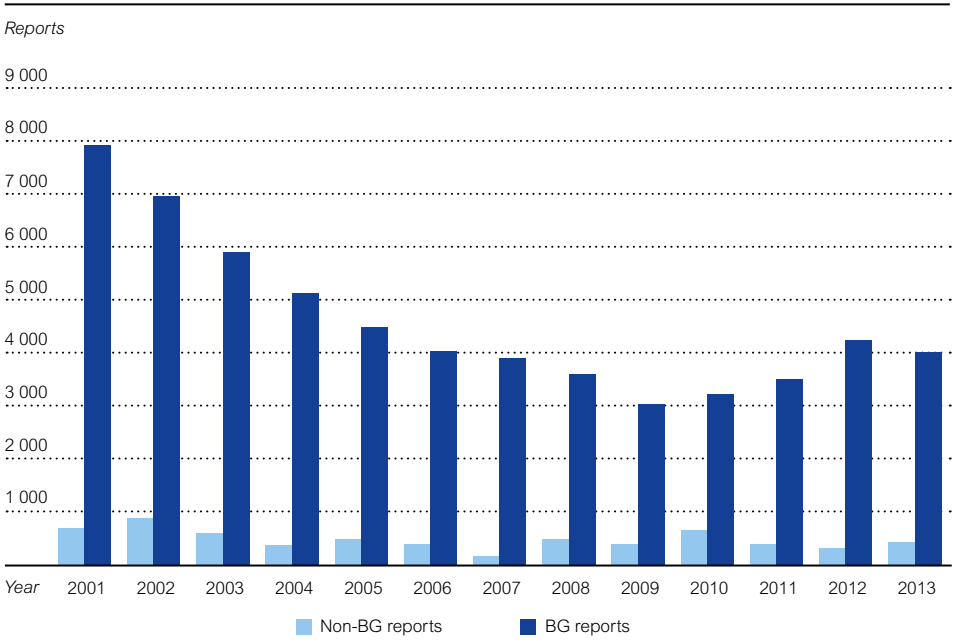

Fig. 33: Cases reported

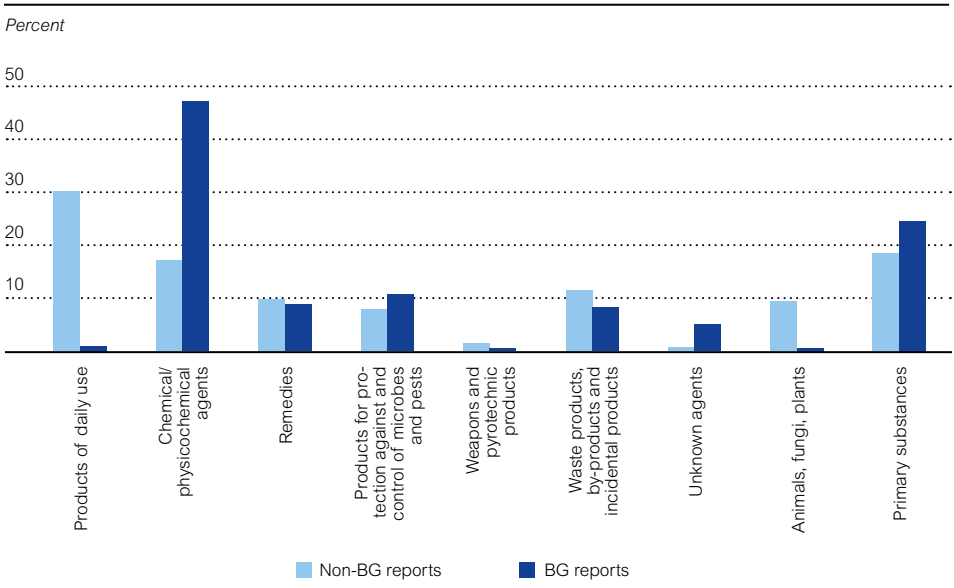

Fig. 34: Spectrum of cases reported in 2011 – 2013 (repeat listing of toxic agents per case possible)

Among the reports submitted by hospitals, medical practitioners and other non-BG reporters during the 2011–2013 period, 67 % referred to cases of accidental poisoning, followed by exposure during proper use (14 %). Confusion of products/substances was reported in about 2.5 %, and suicidal action, in about 4 % of cases. About 9 % of cases were due to abuse of substances. In the remaining cases, the circumstances of exposure have remained unknown.

5.2.4 Age structure and sex distribution

About 1 % of cases of poisoning reported by the Berufsgenossenschaften referred to children. These case reports described accidents that had occurred in kindergartens or schools. 99 % of cases reported by BGs referred to adults.

Also among the reports submitted by hospitals and medical practitioners, the share of cases in adults was much higher (60 %) than that of cases in children (35 %). In 5 % of cases, the age was not stated.

5.2.5 Degree of severity of health impairment

Also in 2011–2013, the majority of cases reported referred to minor health impairment only, applying to both the cases reported by the Berufsgenossenschaften and those reported by hospitals and medical practitioners. Cases of moderate and severe health impairment were more often reported by medical practitioners and physicians working in hospitals (Table 4).

The product groups involved most frequently with regard to the degree of severity of health effects have been listed in Table 5 for the cases reported by the Berufsgenossenschaften, and in Table 6 for the cases reported by hospitals, medical practitioners and other non-BG reporters. The differences in the spectrum of toxic agents reported are due to differences regarding the availability of such agents in the private sphere and at the workplace, among other reasons.

The relatively high share of reports on cleaning agents submitted by the Berufsgenossenschaften as compared to those submitted by

Health impairment	BG reports			Non-BG reports		
	2011 (3 568 cases)	2012 (4 320 cases)	2013 (4 064 cases)	2011 (439 cases)	2012 (372 cases)	2013 (462 cases)
None	3.8 % (137)	3.6 % (154)	1.5 % (61)	8.1 % (36)	16.7 % (62)	4.8 % (22)
Minor	87.2 % (3 107)	87.6 % (3 783)	89.1 % (3 620)	69.5 % (308)	55.1 % (205)	70.6 % (327)
Moderate	4.8 % (171)	4.8 % (207)	5.5 % (224)	10.4 % (46)	14.5 % (54)	6.7 % (31)
Severe	0.3 % (9)	0.1 % (3)	0.1 % (6)	5.4 % (24)	4.8 % (18)	4.1 % (19)
Cannot be assessed	4.0 % (144)	4.0 % (173)	3.8 % (153)	6.5 % (29)	8.9 % (33)	13.8 % (64)

Table 4: Degree of severity of health impairment according to PSS

Product group	Health impairment								
	Minor			Moderate			Severe		
	2011	2012	2013	2011	2012	2013	2011	2012	2013
Primary substances	737	991	756	51	67	59	6	1	3
Cleaning and maintenance products	687	853	885	33	62	61	-	-	2
Cleaners for rooms, home furnishings and personal items	61	36	61	1	1	3	-	-	-
Cleaners for bathrooms and sanitary facilities	39	62	86	4	6	5	-	-	-
Cleaners for kitchens and kitchen appliances	78	83	99	8	12	6	-	-	-
Cleaners and maintenance products for vehicles	26	23	15	-	2	1	-	-	-
Cleaners for technical appliances and processes including metal processing	60	79	63	2	7	6	-	-	-
Cleaners with specific composition designed to work for specific contaminations	140	180	189	8	11	23	-	-	1
Detergents, cleaning and maintenance products for textiles and leather goods	13	23	15	1	-	-	-	-	-
Cleaners and auxiliary products – miscellaneous	243	341	347	10	21	18	-	-	-
Biocidal material protection agents, hygiene products and disinfectants	331	315	363	12	7	10	-	-	-
Medicinal products/medical devices	268	272	319	3	2	2	-	-	-
Chemicals for technical appliances, processes and products	246	279	300	10	11	16	1	-	-
Construction materials, sealants and adhesives	198	308	329	26	39	40	1	1	-
Waste products, by-products, and incidental products	176	232	222	7	8	16	-	-	-
Paints, varnishes and dyes	105	145	120	5	3	3	-	-	-
Plant protection and pest control products	57	69	33	2	1	-	-	-	-
Chemical/physicochemical agents – unclassified	52	49	62	2	2	3	1	-	-
Cosmetics	49	45	34	1	1	2	-	-	-
Products for plants and animals	4	7	2	-	-	2	-	1	-

Table 5: Product groups involved most frequently, by degree of severity of health impairment (BG reports)

Product group	Health impairment								
	Minor			Moderate			Severe		
	2011	2012	2013	2011	2012	2013	2011	2012	2013
Primary substances	32	61	22	3	8	4	-	5	2
Cleaning and maintenance products	33	16	15	6	4	3	4	1	1
Cleaners for bathrooms and sanitary facilities	4	7	1	3	1	1	2	1	-
Cleaners for kitchens and kitchen appliances	6	1	2	-	2	-	1	-	-
Cleaners with specific composition designed to work for specific contaminations	9	2	1	1	-	-	1	-	-
Detergents, cleaning and maintenance products for textiles and leather goods	6	4	6	1	1	1	-	-	1
Biocidal material protection agents, hygiene products and disinfectants	4	3	3	1	-	2	-	2	2
Medicinal products/medical devices	32	16	15	8	8	1	2	3	1
Chemicals for technical appliances, processes and products	7	14	8	1	2	4	-	-	-
Waste products, by-products, and incidental products	63	18	23	2	4	6	4	2	3
Paints, varnishes and dyes	10	2	4	-	-	-	4	-	-
Plant protection and pest control products	11	16	12	-	7	3	2	1	3
Foods	34	27	36	18	16	10	4	2	-
Mushrooms (fungi)	-	3	1	1	1	-	-	1	5
Drugs of abuse	8	3	2	4	-	-	1	-	-
Plants	5	7	3	-	5	1	-	1	1
Animals	6	1	2	2	-	-	1	-	-
Cosmetics	7	9	13	1	1	-	1	-	-
Objects of daily use	1	3	143	-	1	1	-	-	-
Tobacco products	-	7	10	-	1	1	-	-	2

Table 6: Product groups involved most frequently, by degree of severity of health impairment (non-BG reports)

hospitals and medical practitioners has mainly to be attributed to the reporting of cases involving industrial and milking machine cleaners. As expected, BG reports were dominated by occupation-specific risk factors (Table 5). As in previous years, the non-BG reports showed a relatively high share of poisonings caused by cleaning agents (Table 6).

5.2.6 Outcome of cases

In the 2011 – 2013 period, cases characterized by possible late sequelae or incomplete healing accounted for 8 % of all cases reported by the Berufsgenossenschaften. In all other cases, a complete restoration of health could be expected.

Among the reports submitted by hospitals, medical practitioners and other non-BG reporters, cases with possible late sequelae or incomplete healing accounted for 2.5 % of all cases.

In 2011, altogether four deaths were reported to BfR.

- A 76-year old male died from carbon monoxide poisoning after an apartment fire, in spite of repeated resuscitation efforts.
- Another elderly male had ingested 250 mL of a hand dishwashing detergent with a suicidal intent. In spite of intensive therapy, he died from pulmonary oedema within 24 hours.
- Another male had suffered extensive burns and confirmed smoke inhalation injury during an apartment fire. Both the cyanide and carbon monoxide levels in his blood had caused severe poisoning. The patient eventually died in spite of initially successful resuscitation.
- An elderly female who had been suffering from severe depression had ingested about 500 mL of an acid-containing lavatory cleaner with a suicidal intent. She suffered chemical burns in her oesophagus and stomach. In addition, she developed toxic pulmonary oedema and eventually, died from multiple organ failure.

In 2012, altogether five deaths were reported to BfR.

- A 91-year-old female died from the sequelae of chemical burns due to an alkali-containing drain cleaner.
- A young male died from carbon monoxide poisoning after accidental inhalation of exhaust gases from machinery powered by an internal combustion engine. The exhaust gases entered an insufficiently ventilated room where the young male had gone to sleep.
- Three workers who had to wear protective suits with air supply during their working operations died from oxygen deficiency. A defective air supply was discussed as a possible cause. This case was first submitted to BfR as ammonia poisoning. Further investigations and information on this case eventually revealed a defective air supply to have been the cause of the deaths.

In 2013, altogether four deaths were reported to BfR.

- A 6-year-old boy died after drinking from a bottle containing an initially unknown liquid. Further investigations revealed that an organophosphate-based insecticide had been filled into the bottle.
- An infant died from respiratory depression after fentanyl poisoning. The fentanyl had originated from a fentanyl-based pain relief patch that had inadvertently been placed within reach of the child in the home. The child had put the patch into his mouth.

- A 41-year-old male died from methanol poisoning. The male who had a long history of alcohol addiction had ingested methanol with a suicidal intent and suffered an epileptic seizure (grand mal seizure). Subsequently, he fell into a coma and eventually, died from brain death.

- The last death reported referred to an animal and had occurred after administration of a veterinary medicinal product. The cat died after administration of a product containing neem tree seed extract. No more details were available on this case.

5.3 The product information system, PRINS

In order to protect consumers from health risks posed by chemicals and chemical products, the reports by physicians in cases of poisoning legally required under the Chemicals Act (§ 16e para 2) are regularly evaluated in the sense of toxicological monitoring. Since 1994, the reporting physicians, the responsible ministries and the scientific community have been informed by annual reports on the analyses of such reports and their results. In the context of these reports, the term of 'poisoning' is used to designate any health impairment associated with chemicals, i.e. not only severe or potentially fatal conditions but also undesirable health effects of products such as allergic symptoms and allergies.

Since 1998, manufacturers and distributors of chemical products such as household chemicals and DIY products, cosmetics, plant protection and pest control products and products for commercial use have been informed about selected and defined cases of health impairment associated with their products that have become known to BfR through case reports by physicians. For this purpose, a formal product information system (PRINS) was established. If health impairment is reported, rapid communications are provided for in such defined cases, depending on the urgency of measures to be taken. By such approach, industry is enabled to immediately fulfil their obligations with regard to product safety. All other reports are summarized and sent to the recipients mentioned above at annual intervals.

Rapid communication

If reports on severe health risks are received by BfR, and a preparation is suspected of possibly involving a risk, BfR will provide for submission of information not only to the manufacturer/distributor of the chemical product involved, but also to the competent industrial association/federal trade association. In addition, such rapid communication is submitted to the three competent ministries, i.e. the Federal Ministry of Food and Agriculture, the Federal Ministry for the Environment, Nature Conservation and Nuclear Safety, and the Federal Ministry of Health. Suicides, abuse and improper use are excluded from the obligation to submit rapid communications.

Criteria for a rapid communication include

- Severe symptomatology;
- No suicide or abuse; and
- No improper use.

In the period between 1 January 1998 and 31 December 2010, 31 rapid communications were processed.

As agreed, no rapid communications were issued by BfR in spite of severe health impairments reported because there was obviously no need for action by the manufacturers involved. The manufacturers were informed about the accidents later in summarized form.

For explanations of individual cases up to 2010, reference is made to the previous annual reports.

Summary reports

Information on reports referring to cases of non-severe health impairment caused by chemical products in occupational or private environments is transmitted to the responsible manufacturers/distributors in a summarized form at the beginning of the year following the incidents. Since 2003, also suicides and attempted suicides have been included in the summary reports, irrespective of the degree of severity of poisoning. Rarely, also reports of severe cases are submitted to manufacturers in the form of a summary report if the data available were insufficient for a rapid communication.

Summary reports provide information on the data of the corresponding case reports in tabular form which will include the following elements:

- Product name;
- Case number;
- Age group;
- Site of exposure (workplace or private sphere);
- Duration of exposure (acute or chronic); and
- Degree of severity of health impairment as assessed by BfR.

Cases reported to BfR will only result in a report being sent to the manufacturers if a causal relationship between the health impairment experienced and the product mentioned is considered at least as possible after evaluation by BfR. Information is also submitted on cases reported for which the degree of severity and/or the causal relationship cannot be assessed. Also in these cases, it is intended to draw the manufacturers' attention to risks that may arise from their products.

By means of the BfR summary reports, manufacturers and distributors are informed about possible risks associated with the handling of their products. In single cases, they will not be satisfied by such summarized information and seek contact with the BfR in writing or by telephone in order to obtain more detailed information on a specific case of poisoning.

Table 7 shows the number of such summary reports sent to the corresponding manufacturers after evaluation of all reports on cases of poisoning received by BfR in the 2011 to 2013 period according to the criteria explained above. In some cases, several products were mentioned to have been involved as toxic agents in one report. Therefore, the total number of products listed for summary reports is higher than that of the corresponding reports on cases of poisoning.

Table 8 shows the degrees of severity of the cases of health impairment reported.

Year	2011	2012	2013
Cases reported, total	4 007	4 692	4 526
Cases for summary reports	**351**	**410**	**524**
No. of products	368	422	528
No. of manufacturers addressed	160	171	147

Table 7: Summary reports to manufacturers, synoptic table (repeat listing of toxic agents per case possible)

Degree of severity/year	2011	2012	2013
Minor	313	370	478
Moderate	17	27	28
Severe	7	1	4
Cannot be assessed	14	12	14
Moderate and severe cases	6.8 %	6.8 %	6.1 %

Table 8: Degree of severity of cases referred to in summary reports to manufacturers

Product groups	No. of reports		
	2011	2012	2013
Products of daily use	**9**	**15**	**147**
Objects of daily use (except cleaning and indoor air conditioning agents)		3	144
• Toys and joke articles		3	144
Cosmetics	9	12	3
• Skin care products	3	6	2
• Hair care products	3	4	
• Oral hygiene products	3	2	
Chemical/physicochemical agents	**200**	**219**	**224**
Construction materials, sealants and adhesives	11	12	16
• Building and auxiliary materials, sealants	5	8	11
• Glues	6	3	5
Paints, varnishes and dyes	18	9	11
• Paint coats, varnishes and primers	17	9	11
Cleaning and maintenance products	145	178	164
• Cleaners for rooms, home furnishings and personal items	9	17	26
• Cleaners for bathrooms and sanitary facilities	20	22	18
• Cleaners for kitchens and kitchen appliances (incl. dishes, metallic objects)	23	26	24
• Cleaners and maintenance products for vehicles	3	4	3
• Cleaners for technical appliances and processes including metal processing	27	34	30
• Cleaners and maintenance products for stones, facades, building parts	3	4	5
• Cleaners with specific composition designed to work for specific contaminations	41	49	45
• Detergents, cleaning and maintenance products for textiles and leather goods	7	4	5
• Cleaners and auxiliary products - miscellaneous	4	4	4
• Cleaners and auxiliary products - unclassified	8	14	4
Chemicals for technical appliances, processes and products	22	16	29
• Technical products containing chemical substances		5	1

Product groups	No. of reports		
	2011	2012	2013
• Equipment for vehicles and machinery	4	11	10
• Chemical-technical processing and production aids	16		18
Products for plants and animals	2	3	3
• Pet shop products	2	3	2
Remedies	**37**	**46**	**32**
Medical devices	37	46	32
• Disinfectants, cleaners and maintenance products for medical devices	35	44	31
Products for protection against and control of microbes and pests	**118**	**136**	**122**
Biocidal material protection agents, hygiene products and disinfectants	94	106	101
• Disinfectants and biocidal hygiene products	91	93	88
• Biocides for food and feedstuffs		3	1
• Biocidal preservatives for wood and structures		3	3
• Biocidal preservatives for products, processes and other special purposes	3	6	8
Plant protection and pest control products	24	30	21
• Plant protection products for systemic application	20	23	18
• Pest control products and repellents	4	7	3
Man-made products - unclassified	**4**	**6**	**3**
Primary substances	3	6	3
Man-made products – total number of reports	**368**	**422**	**528**

Table 9: Product groups involved in 2010-2013 summary reports (minimum three listings per product group within at least one year)

Table 9 provides a synoptic view of the product application groups of the Society of Clinical Toxicology (Gesellschaft für Klinische Toxikologie e.V.) to which the products referred to in the summary reports can be assigned.

As in the previous period, the majority of reports referred to accidents involving chemical/physicochemical agents, with cleaning and maintenance products stated most frequently. Also the number of case reports referring to products for protection against and control of microbes and pests has remained high, with particular emphasis on disinfectants and biocidal hygiene products.

Product groups	Health impairment					
	Moderate			Severe		
	2011	2012	2013	2011	2012	2013
Toys and joke articles		1	1		1	
Hair care products	1					
Building and auxiliary materials, sealants	1		2			
Glues		2				
Paint coats, varnishes and primers				2		
Cleaners for bathrooms and sanitary facilities	2	5		2		
Cleaners for kitchens and kitchen appliances (incl. dishes, metallic objects)	2	6	2	1		
Cleaners for technical appliances and processes including metal processing	3	2	3			1
Cleaners with specific composition designed to work for specific contaminations	2	2	8	1		
Detergents, cleaning and maintenance products for textiles and leather goods	2		1			1
Chemical-technical processing and production aids	1	2	3			
Products for plants and cut flowers			1			
Pet shop products		2	1			
Disinfectants, cleaners and maintenance products for medical devices		3				
Disinfectants and biocidal hygiene products	4	2	5			1
Biocidal preservatives for wood and structures						1
Biocidal preservatives for products, processes and other special purposes			1			
Plant protection products for systemic application	1		1			
Pest control products and repellents				1		

Table 10: Product groups associated with cases of moderate and severe health impairment referred to in 2011, 2012 and 2013 summary reports

Table 10 shows the number of products in the individual product groups that were associated with cases of moderate and severe health impairment (repeat listing per case possible).

BfR also performs cumulative data analyses of case reports. If trends become apparent, the manufacturers of the products concerned are informed accordingly. In turn, manufacturers are requested by BfR to communicate comparable data and trends that may serve to improve product safety.

6 Annex

6.1 Standards for the assessment of poisonings

6.1.1 The three-level model

(Cf. Chapter 1.4.)

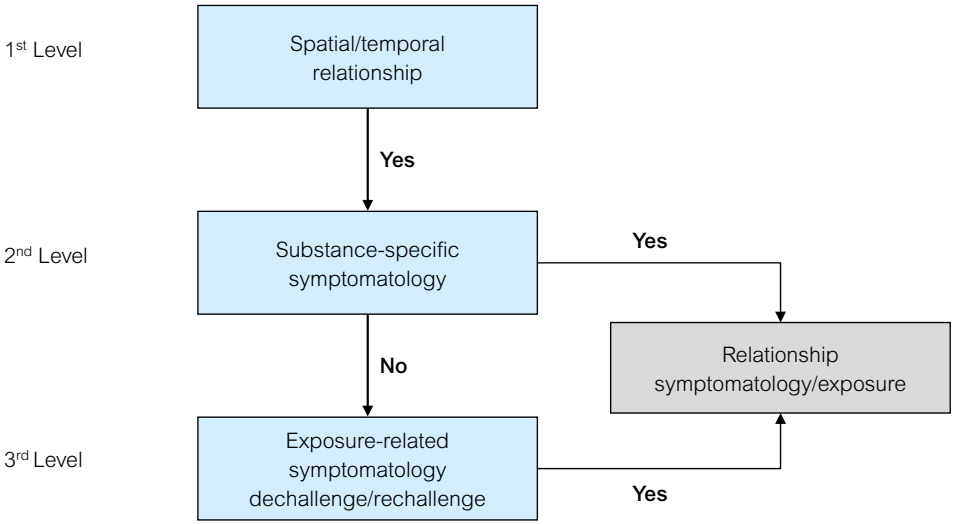

Fig. 35: The three-level model

6.1.2 Matrix to assess the degree of probability of exposure to a substance

(Cf. Chapter 1.4.)

Degree of probability of exposure		Estimation		Measurements			
		Contact with substance		**Extracorporeal**		**Intracorporeal**	
		Source(s)	Potential exposure	Single value	Representative measurements	Single value	Exceeding of limit values
No	None	+	-	-	-	-	-
Yes	Possible/cannot be reliably excluded	+	+	+	-	-	-
	Probable	+	+	+	+	+	-
	Confirmed	+	+	+	+	+	+
?	Cannot be assessed	E.g. insufficient data, state of knowledge					

Table 11: First Step: Matrix to assess the degree of probability of exposure to a substance

6.1.3 Matrix to assess the causal relationship between health disorder/symptomatology and exposure

(Cf. Chapter 1.4.)

Relationship exposure/symptomatology		Plausible exposure to a substance	Partially specific symptoms	Specific symptoms	Specific laboratory analysis	Other diagnosis
No	None	-	-	-	-	+
Yes	Possible/cannot be reliably excluded	+	+	-	-	+
	Probable	+	+	+	-	-
	Confirmed	+	+	+	+	-
?	Cannot be assessed	E.g. insufficient data, state of knowledge				

Table 12: Second Step: Matrix to assess the causal relationship between health disorder/symptomatology and exposure

6.2 Processing of cases of poisoning at BfR

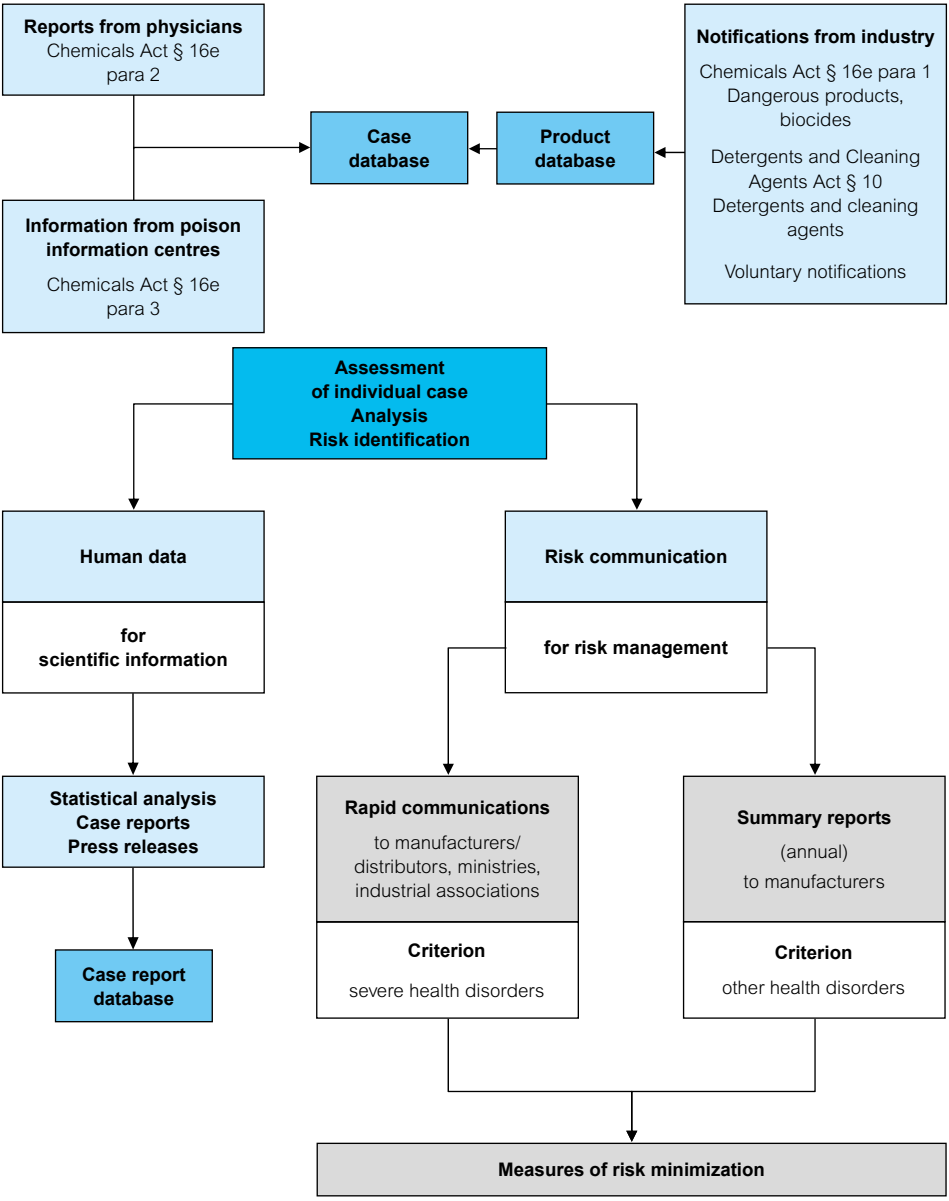

Fig. 36: Terms of reference of the Poisoning and Product Documentation Centre

6.3 Synoptic view of the cases of poisoning reported

Tables 13a-c summarize 69 109 reports (except for cases classified as "no relationship" between symptomatology and exposure) vs. degree of severity of health disturbance.

6.3.1 Cases in adults

Product groups	No. of reports		Health impairment					
	Total	Adults	Asympt.	Minor	Moder-ate	Severe	Fatal	Un-known
Man-made products	**69 109**	**64 561**	**1 701**	**54 259**	**5 692**	**558**	**188**	**2 163**
Products of daily use	3 151	2 554	34	2 024	338	64	22	72
• Objects of daily use (except cleaning and indoor air conditioning agents)	663	474	5	407	52	4		6
• Cosmetics	1 104	935	10	805	89	5	4	22
• Foods and food additives	1 263	1 145	15	835	200	35	18	42
• Tobacco products	175	54	4	19	5	24		2
• Products of daily use – unclassified	1	1			1			
Chemical/physicochemical agents	29 058	27 123	402	23 583	2 141	134	34	829
• Construction materials, sealants and adhesives	4 323	4 235	34	3 621	454	8	1	117
• Paints, varnishes and dyes	3 047	2 964	59	2 574	198	23	5	105
• Lamp fuels, lighting, odoriferous, decorative and related chemical agents	1 206	220	8	165	24	11	4	8
• Cleaning and maintenance products	13 692	13 074	158	11 356	1 067	57	19	417
• Chemicals for technical appliances, processes and products	5 482	5 346	125	4 738	305	28	4	146
• Products for plants and animals	231	220	1	175	28	2		14
• Chemical/physicochemical agents – unclassified	1 317	1 302	19	1 145	95	11	3	29

Table 13a: Spectrum of cases of poisoning reported until 2013, by product groups of the Society of Clinical Toxicology e.V. (adults)

Product groups	No. of reports		Health impairment					
	Total	Adults	Asympt.	Minor	Moder-ate	Severe	Fatal	Un-known
Drugs of abuse	124	118		51	39	17	3	8
• Aphrodisiacs	2	2		1			1	
• Centrally active sedatives	75	72		28	22	14	1	7
• Hallucinogens	9	8		4	3	1		
• Psychostimulants	19	17		4	8	3	1	1
• Drugs of abuse – unclassified	27	27		17	9			1
Remedies	5 206	4 335	236	3 483	325	110	26	155
• Medicinal products (for human use)	3 398	2 562	198	1 981	192	87	18	86
• Medical devices	1 644	1 628	36	1 386	118	20	5	63
• Veterinary medicines	176	156	4	124	15	4	3	6
• Remedies – unclassified	2	2			2			
Products for protection against and control of microbes and pests	7 918	7 646	160	6 324	708	108	68	278
• Biocidal material protection agents, hygiene products and disinfectants	5 208	5 128	88	4 544	324	28	4	140
• Plant protection and pest control products	2 733	2 540	72	1 788	395	82	64	139
• Products for protection against and control of microbes and pests – unclassified	8	8		8				
Weapons and pyrotechnic products	353	276	18	235	14	1		8
• Pyrotechnic products – civil use	13	7		4	2			1
• Weapons and special products for military use	339	269	18	231	12	1		7
• Weapons and pyrotechnic products – unclassified	1							

Table 13a continued: Spectrum of cases of poisoning reported until 2013, by product groups of the Society of Clinical Toxicology e.V. (adults)

Product groups	No. of reports		Health impairment					
	Total	Adults	Asympt.	Minor	Moder-ate	Severe	Fatal	Un-known
Man-made products – unclassified	24 890	24 052	867	19 629	2 435	196	58	867
• Primary substances	23 114	22 290	842	18 090	2 318	193	58	789
Natural environment	**637**	**361**	**16**	**232**	**68**	**22**	**7**	**16**
Mushrooms (fungi)	135	98	4	49	22	18	1	4
• Eumycota	94	66	4	22	21	17	1	1
• Fungi – unclassified	42	33		27	2	1		3
Microbes	68	4		4				
Plants	316	147	5	91	32	4	5	10
• Spermatophyta	301	136	5	80	32	4	5	10
• Plants – unclassified	11	8		8				
Animals	55	49		37	11	1		
• Arthropoda – Tracheata	8	7		6	1			
• Chordata – Vertebrata	17	13		8	5			
Natural environment – miscellaneous/unclassified	67	67	7	54	3		1	2
Civilization-associated and inherited wastes	**5 014**	**4 918**	**402**	**3 925**	**318**	**44**	**42**	**187**
Waste products, by-products, and incidental products	4 998	4 903	398	3 916	317	43	42	187
• Waste products and by-products – regular	1 774	1 731	66	1 345	192	31	21	76
• Reaction products from accident/breakdown/fire	3 047	2 997	330	2 414	118	6	22	107
• Waste products, by-products and incidental products – unclassified	197	195	3	170	11	6		5
Civilization-associated and inherited wastes – unclassified	16	15	4	9	1	1		
Unclassified/unknown items	**3 001**	**2 976**	**98**	**2 549**	**192**	**9**		**128**
Unknown agent	**2 540**	**2 518**	**79**	**2 181**	**146**	**4**		**108**
Unknown category	**468**	**465**	**19**	**374**	**46**	**5**		**21**

Table 13a continued: Spectrum of cases of poisoning reported until 2013, by product groups of the Society of Clinical Toxicology e.V. (adults)

6.3.2 Cases in children

Product groups	No. of reports		Health impairment					
	Total	Adults	Asympt.	Minor	Moder-ate	Severe	Fatal	Un-known
Man-made products	**69 109**	**4 223**	**959**	**2 308**	**634**	**93**	**15**	**214**
Products of daily use	3 151	548	117	351	43	10	2	25
• Objects of daily use (except cleaning and indoor air conditioning agents)	663	186	7	164	11	2		2
• Cosmetics	1 104	160	44	92	11	2	1	10
• Foods and food additives	1 263	83	7	46	18	6	1	5
• Tobacco products	175	119	59	49	3			8
• Products of daily use – unclassified	1							
Chemical physicochemical agents	29 058	1 873	392	925	415	45	7	89
• Construction materials, sealants and adhesives	4 323	80	8	61	9			2
• Paints, varnishes and dyes	3 047	77	12	43	15	3		4
• Lamp fuels, lighting, odoriferous, decorative and related chemical agents	1 206	980	137	455	323	26	5	34
• Cleaning and maintenance products	13 692	598	192	301	57	13		35
• Chemicals for technical appliances, processes and products	5 482	116	39	50	11	3	2	11
• Products for plants and animals	231	10	3	5				2
• Chemical/physicochemical agents – unclassified	1 317	14	1	11		1		1
Drugs of abuse	124	2		1	1			
• Aphrodisiacs	2							
• Centrally active sedatives	75	1		1				

Table 13b: Spectrum of cases of poisoning reported until 2013, by product groups of the Society of Clinical Toxicology e.V. (children)

Product groups	No. of reports		Health impairment					
	Total	Adults	Asympt.	Minor	Moder-ate	Severe	Fatal	Un-known
• Hallucinogens	9	1			1			
• Psychostimulants	19							
• Drugs of abuse – unclassified	27							
Remedies	5 206	844	308	347	105	25	2	57
• Medicinal products (for human use)	3 398	817	301	339	95	24	2	56
• Medical devices	1 644	11	3	1	6	1		
• Veterinary medicines	176	17	5	7	4			1
• Remedies – unclassified	2							
Products for protection against and control of microbes and pests	7 918	266	70	146	24	6	1	19
• Biocidal material protection agents, hygiene products and disinfectants	5 208	80	19	46	9	1		5
• Plant protection and pest control products	2 733	187	51	101	15	5	1	14
• Products for protection against and control of microbes and pests – unclassified	8							
Weapons and pyrotechnic products	353	75	4	67	3	1		
• Pyrotechnic products – civil use	13	6	1	4		1		
• Weapons and special products for military use	339	68	3	62	3			
• Weapons and pyrotechnic products – unclassified	1	1		1				
Man-made products – unclassified	24 890	654	78	485	52	11	3	25
• Primary substances	23 114	641	77	480	52	11	3	18

Table 13b continued: Spectrum of cases of poisoning reported until 2013, by product groups of the Society of Clinical Toxicology e.V. (children)

Product groups	No. of reports		Health impairment					
	Total	Adults	Asympt.	Minor	Moder-ate	Severe	Fatal	Un-known
Natural environment	**637**	**266**	**100**	**142**	**6**	**6**		**12**
Mushrooms (fungi)	135	34	15	11	2	5		1
• Eumycota	94	26	9	9	2	5		1
• Fungi – unclassified	42	8	6	2				
Microbes	68	64		64				
Plants	316	163	85	64	2	1		11
• Spermatophyta	301	159	84	61	2	1		11
• Plants – unclassified	11	3		3				
Animals	55	5		3	2			
• Arthropoda – Tracheata	8	1		1				
• Chordata – Vertebrata	17	4		2	2			
Natural environment – miscellaneous/unclassified	67							
Civilization-associated and inherited wastes	**5 014**	**80**	**9**	**46**	**12**	**1**	**1**	**11**
Waste products, by-products, and incidental products	4 998	79	9	46	11	1	1	11
• Waste products and by-products – regular	1 774	34	1	17	8	1		7
• Reaction products from accident/breakdown/fire	3 047	43	8	27	3		1	4
• Waste products, by-products and incidental products – unclassified	197	2		2				
Civilization-associated and inherited wastes – unclassified	16	1			1			
Unclassified/unknown items	**3 001**	**11**	**3**	**4**	**1**	**2**		**1**
Unknown agent	**2 540**	**8**	**3**	**2**	**1**	**1**		**1**
Unknown category	**468**	**3**		**2**		**1**		

Table 13b continued: Spectrum of cases of poisoning reported until 2013, by product groups of the Society of Clinical Toxicology e.V. (children)

6.3.3 Cases with no record of age

Product groups	No. of reports		Health impairment					
	Total	Adults	Asympt.	Minor	Moder-ate	Severe	Fatal	Un-known
Man-made products	**69 109**	**325**	**42**	**207**	**18**	**3**	**1**	**54**
Products of daily use	3 151	49	3	39	4	2		1
• Objects of daily use (except cleaning and indoor air conditioning agents)	663	3		2	1			
• Cosmetics	1 104	9	2	7				
• Foods and food additives	1 263	35		30	3	1		1
• Tobacco products	175	2	1			1		
• Products of daily use – unclassified	1							
Chemical/physicochemical agents	29 058	62	19	27	9	1		6
• Construction materials, sealants and adhesives	4 323	8		6	2			
• Paints, varnishes and dyes	3 047	6	2	3	1			
• Lamp fuels, lighting, odoriferous, decorative and related chemical agents	1 206	6		5				1
• Cleaning and maintenance products	13 692	20		9	6	1		4
• Chemicals for technical appliances, processes and products	5 482	20	16	3				1
• Products for plants and animals	231	1	1					
• Chemical/physicochemical agents – unclassified	1 317	1		1				
Drugs of abuse	124	4		2		1		1
• Aphrodisiacs	2							
• Centrally active sedatives	75	2				1		1

Table 13c: Spectrum of cases of poisoning reported until 2013, by product groups of the Society of Clinical Toxicology e.V. (age unknown)

Product groups	No. of reports		Health impairment					
	Total	Adults	Asympt.	Minor	Moder-ate	Severe	Fatal	Un-known
• Hallucinogens	9							
• Psychostimulants	19	2		2				
• Drugs of abuse – unclassified	27							
Remedies	5 206	27	5	12	3		1	6
• Medicinal products (for human use)	3 398	19	3	9	2			5
• Medical devices	1 644	5	1	2	1			1
• Veterinary medicines	176	3	1	1			1	
• Remedies – unclassified	2							
Products for protection against and control of microbes and pests	7 918	6		3	2			1
• Biocidal material protection agents, hygiene products and disinfectants	5 208							
• Plant protection and pest control products	2 733	6		3	2			1
• Products for protection against and control of microbes and pests – unclassified	8							
Weapons and pyrotechnic products	353	2	1	1				
• Pyrotechnic products – civil use	13							
• Weapons and special products for military use	339	2	1	1				
• Weapons and pyrotechnic products – unclassified	1							
Man-made products – unclassified	24 890	184	14	128	2	1		39
• Primary substances	23 114	183	13	128	2	1		39

Table 13c continued: Spectrum of cases of poisoning reported until 2013, by product groups of the Society of Clinical Toxicology e.V. (age unknown)

Product groups	No. of reports		Health impairment					
	Total	Adults	Asympt.	Minor	Moder-ate	Severe	Fatal	Un-known
Natural environment	**637**	**10**	**1**	**6**	**1**			**2**
Mushrooms (fungi)	135	3	1	1				1
• Eumycota	94	2	1	1				
• Fungi – unclassified	42	1						1
Microbes	68							
Plants	316	6		4	1			1
• Spermatophyta	301	6		4	1			1
• Plants – unclassified	11							
Animals	55	1		1				
• Arthropoda – Tracheata	8							
• Chordata – Vertebrata	17							
Natural environment – miscellaneous/unclassified	67							
Civilization-associated and inherited wastes	**5 014**	**16**		**12**	**2**			**2**
Waste products, by-products, and incidental products	4 998	16		12	2			2
• Waste products and by-products – regular	1 774	9		8	1			
• Reaction products from accident/breakdown/fire	3 047	7		4	1			2
• Waste products, by-products and incidental products – unclassified	197							
Civilization-associated and inherited wastes – unclassified	16							
Unclassified/unknown items	**3 001**	**14**	**1**	**11**				**2**
Unknown agent	**2 540**	**14**	**1**	**11**				**2**
Unknown category	**468**							

Table 13c continued: Spectrum of cases of poisoning reported until 2013, by product groups of the Society of Clinical Toxicology e.V. (age unknown)

6.4 Reporting form for cases of poisoning

Bundesinstitut für Risikobewertung
Vergiftungs- und Produktdokumentation
Postfach 12 69 42

10609 Berlin

Stempel, Telefon-Nummer und Unterschrift der/des Ärztin/Arztes

Mitteilung bei Vergiftungen
nach § 16 e Abs. 2 des Chemikaliengesetzes
Telefon: 030 18412-3460, Fax: 030 18412-3929, E-Mail: giftdok@bfr.bund.de

1. Angaben zur/zum Patientin/en:

Alter: Jahre ☐ Monate (bei Kindern unter 3 Jahren) ☐ ☐ ☐ männlich ☐ weiblich **Schwangerschaft** (**freiwillig** auszufüllen) ☐ ja ☐ nein

2. Vergiftung ☐ **Verdacht** ☐

Unbedingt Handelsname der Zubereitung/des Biozid-Produktes oder Stoffname, aufgenommene Menge und Hersteller (Vertreiber); ggf. vermutete Ursache

a.

b.

c.

3. Exposition ☐ akut ☐ chronisch ☐ oral ☐ inhalativ ☐ Haut ☐ Auge ☐ sonstiges welche

Art der Vergiftung:	☐ akzidentell (Unfall)	☐ gewerblich	☐ Verwechslung	
	☐ suizidale Handlung	☐ Abusus	☐ Umwelt	☐ Sonstiges
Ort:	☐ Arbeitsplatz	☐ im Haus	☐ Schule	
	☐ Kindergarten	☐ im Freien	☐ Sonstiges	
Labor-Nachweis:	☐ ja	☐ nein		
Behandlung:	☐ keine	☐ ambulant	☐ stationär	
Verlauf:	☐ nicht bekannt	☐ vollständige Heilung	☐ Defektheilung	☐ Tod
	☐ Spätschäden (nicht auszuschließen)			

4. Symptome, Verlauf – stichwortartig – (ggf. anonymisierte Befunde, Epikrise beilegen) (**freiwillig** auszufüllen)

6.5 Reporting form for industrial accidents

BfR-Fragebogen zur Expositionsermittlung bei Stör- und Transportunfällen

Pers. Nummer ☐

weiblich ☐ männlich ☐ Erwachsene(r) ☐ Kind ☐

Bereich I

Unmittelbar Betroffene(r)

(Bitte Eintrag in die Landkarte)

Direkt am Unfallort ☐

Nahe Unfallort ☐

☐ m

Arbeiter(in) ☐

Feuerwehr ☐

Polizei/Rettungsdienst ☐

Privatperson ☐

Sonstige(r) ☐

Erstexposition Uhrzeit ☐ Datum ☐

Dauer ständig ☐ nicht ständig Stunden/Tage ☐

Schutzmaßnahmen ja ☐ nein ☐

Symptome ja ☐ nein ☐

(Wenn ja, bitte Dokumentation auf dem Meldebogen)

Bereich II

Nicht unmittelbar Betroffene(r)

(Bitte Eintrag in die Landkarte)

Entfernung vom Unfallort

☐ m

☐ km

Anwohner ☐

Beschäftigte(r)/Arbeitnehmer(in) ☐

Sonstige(r) ☐ ☐

Erstexposition Uhrzeit ☐ Datum ☐

Dauer ständig ☐ nicht ständig Stunden/Tage ☐

Symptome ja ☐ nein ☐

(Wenn ja, bitte Dokumentation auf dem Meldebogen)

Biomonitoring **Stoff:** ☐

Blutentnahme ☐ Datum ☐ Zeitpunkt ☐ Konzentration ☐

Urinprobe ☐ Datum ☐ Zeitpunkt ☐ Konzentration ☐

Spontanurin ☐ 24h Sammelurin ☐ Kreatinin ☐

6.6 List of poison information centres in Germany (status as of January 2015)

Berlin	Universitätsklinikum Charité Giftnotruf (poison emergency hotline) CBF, Haus VIII (Wirtschaftsgebäude), UG	Hindenburgdamm 30	12203 Berlin	Emergency hotline: +49-30-19 24 0 Fax: +49-30-30 686 799 mail@giftnotruf.de www.giftnotruf.de
Bonn	Informationszentrale gegen Vergiftungen Zentrum für Kinderheilkunde Universitätsklinikum Bonn	Adenauerallee 119	53113 Bonn	Emergency hotline: +49-228-19 24 0 Fax: +49-228-28 7-3 32 78 oder +49-228-28 7-3 33 14 gizbn@ukb.uni-bonn.de www.gizbonn.de
Erfurt	Giftnotruf Erfurt Gemeinsames Giftinformationszentrum der Länder Mecklenburg-Vorpommern, Sachsen, Sachsen-Anhalt und Thüringen (GGIZ) c/o HELIOS Klinikum Erfurt	Nordhäuser Straße 74	99089 Erfurt	Phone: +49-361-73 07 30 Fax: +49-361-73 07 31 7 ggiz@ggiz-erfurt.de www.ggiz-erfurt.de
Freiburg	Zentrum für Kinder- und Jugendmedizin Vergiftungs-Informations-Zentrale Freiburg (VIZ)	Mathildenstraße 1	79106 Freiburg	Emergency hotline: +49-761-19 24 0 Fax: +49-761-27 0-4 45 70 giftinfo@uniklinik-freiburg.de www.giftberatung.de
Göttingen	Giftinformationszentrum-Nord der Länder Bremen, Hamburg, Niedersachsen und Schleswig-Holstein (GIZ-Nord) Universitätsmedizin Göttingen Georg-August-Universität	Robert-Koch-Straße 40	37075 Göttingen	Emergency hotline: +49-551-19 24 0 Fax: +49-551-38 31 88 1 giznord@giz-nord.de www.Giz-Nord.de

Homburg	Informations- und Beratungszentrum für Vergiftungsfälle Klinik für Kinder- und Jugendmedizin Universitätsklinikum des Saarlandes, Gebäude 9	Kirrberger Straße 100	66421 Homburg/ Saar	Emergency hotline: +49-6841-19 24 0 Office: +49-6841-16 28 436 Fax: +49-6841-16 21 109 giftberatung@uniklinikum-saarland.de www.uniklinikum-saarland.de/giftzentrale
Mainz	Giftinformationszentrum der Länder Rheinland-Pfalz und Hessen Klinische Toxikologie Universitätsmedizin der Johannes Gutenberg-Universität Mainz Gebäude 601	Langebeck-straße 1	55131 Mainz	Emergency hotline: +49-6131-19 24 0 Infoline: +49-6131-23 24 66 Fax: +49-6131-23 24 68 mail@giftinfo.uni-mainz.de www.giftinfo.uni-mainz.de
München	Giftnotruf München (poison emergency hotline) Toxikologische Abteilung der II. Medizinischen Klinik und Poliklinik des Klinikums rechts der Isar der Technischen Universität München	Ismaninger Straße 22	81675 München	Emergency hotline: +49-89-19 24 0 Fax: +49-89-41 40 24 67 tox@lrz.tu-muenchen.de www.toxinfo.med.tum.de/inhalt/giftnotrufmuenchen

6.7 BfR press releases on toxicological problems issued in the 2011 – 2013 period

Tightening of trade in lamp oils and grill lighter fluids
05/2011, 28 January 2011

Charcoal grills should not be used indoors
19/2011, 23 June 2011

Talc-containing baby powder is a health risk
20/2011, 27.06.2011

Depilatory creams not to be applied extensively 22/2011, 18 July 2011

Risks which get under the skin
26/2011, 01 August 2011

Protecting children from poisoning
35/2011, 14.10.2011

Skull and crossbones for nitric acid
09/2012, 29 February 2012

Dubious herbal mixtures and dangerous mushrooms
10/2012, 02 March 2012

Trend drink bubble tea:
health risk for small children
23/2012, 03 August 2012

Nickel gehört nicht in Tätowiermittel und Permanent Make-up (Nickel has no place in tattoo colorants and permanent make-up, in German only)
15/2013, 06 June 2013

Poisoning accidents among children:
new app facilitates first aid and prevention
24/2013, 22 August 2013

Protecting children from poisoning
26/2013, 18 September 2013

Grilling with charcoal is definitely not an indoor pursuit
27/2013, 01 October 2013

High nickel release from metal construction kits can trigger allergies
30/2013, 12 November 2013

6.8 Abbreviations

Abbreviation	Meaning
µg	Micrograms
µg/mL	Micrograms per millilitre
AAS	Atomic absorption spectrometry
ASH	Alice Salomon Hochschule (Alice Salomon University)
AV-Block	Atrioventricular block
GC	General condition
BAM	Bundesanstalt für Materialforschung und -prüfung (Federal Institute for Materials Research and Testing)
BfR	Bundesinstitut für Risikobewertung (Federal Institute for Risk Assessment)
BG	Berufsgenossenschaft(en) (institution(s) for statutory accident insurance and prevention for trade and industry in Germany)
BK-Nr.	Berufskrankheitsnummer (No. of official registration of occupational diseases)
BVL	Bundesamt für Verbraucherschutz und Lebensmittelsicherheit (Federal Office of Consumer Protection and Food Safety)
ChemG	Chemikaliengesetz (Chemicals Act, Germany)
CLH	Harmonised Classification and Labelling
CLP-Regulation	Regulation (EC) No. 1272/2008 on classification, labelling and packaging of substances and mixtures
CO	Carbon monoxide
COHb	Carboxyhaemoglobin
CT	Computed tomography
EAPCCT	European Association of Poisons Centres and Clinical Toxicologists
ECHA	European Chemicals Agency

Abbreviation	Meaning
EFSA	European Food Safety Authority
ESPED	Erhebungseinheit für seltene pädiatrische Erkrankungen in Deutschland (clinical registration unit for rare paediatric diseases in Germany)
EU	European Union
EU Regulation	Regulation of the European Union
EVA	Erfassung der Vergiftungsfälle und Auswertungen in den Informations- und Behandlungszentren für Vergiftungen (recording of cases of poisoning and evaluation at the poisoning information and treatment centres in the Federal Republic of Germany – EDP application program for the documentation of cases of poisoning)
g/dL	Grams per decilitre
GABA	Gamma-aminobutyric acid, a neurotransmitter
GIZ (PC)	Giftinformationszentrum - Poison information centre in Germany
GOT	Glutamate oxaloacetate transaminase
GPT	Glutamate pyruvate transaminase
H 304	May be fatal if swallowed and enters airways. H statements (hazard statements) are short precautionary statements for hazardous substances
Hb	Haemoglobin
iOS	Operating system
LC-MS/MS	Liquid chromatography and tandem mass spectrometry
LD	Lethal dose
lks.	links
MCI/MI	Methylchloroisothiazolinone/methylisothiazolinone
mg/dL	Milligrams per decilitre

Abbreviation	Meaning
mg/kg	Milligrams per kilogram
mmHg	Millimetres of mercury
mmol/l	Millimoles per litre
m-TCP	Meta-tricresyl phosphate
ng/mL	Nanograms per millilitre
Nano	SI prefix meaning 10-9 (part in a billion)
neg	negative
NemV	Nahrungsergänzungsmittelverordnung (German Ordinance on Food Supplements)
nm	Nanometre
NOx	Nitrogen oxides, nitrous gases or nitrogen oxides
OPIDN	Organophosphorus ester-induced delayed neuropathy
OSHA	Occupational Safety and Health Administration
o-TCP	Ortho-tricresyl phosphate
PDF	Portable Document Format (platform independent document)
PES	Peracetic acid
ph-Wert	Measure of acidity or alkalinity of an aqueous solution
pos	positive
PPD	Paraphenylenediamine
ppm	Parts per million
PRINS	Product information system
PSS	Poisoning severity score
p-TCP	Para-tricresyl phosphate
PVC	Polyvinyl chloride
QTc	Frequency-corrected QT interval

Abbreviation	Meaning
R 65	Harmful: may cause lung damage if swallowed. R phrases (risk phrases) are warnings describing the hazardous characteristics of hazardous substances.
RDS	Respiratory Distress Syndrome
TCP	Tricresyl phosphate
THC	Tetrahydrocannabinol
TDI	In this context: Toxicological Documentation and Information Network
TKS	Product categorization system of the Society of Clinical Toxicology (Gesellschaft für Klinische Toxikologie e.V.)
TMDI	Temporary maximum daily intake
TUM	Technische Universität München (Munich Technical University)
U/L	Units per litre
UFI	Unique formula identifier
VOC	Volatile organic compounds
WRMG	Wasch- und Reinigungsmittelgesetz (Detergents and Cleaning Agents Act, Germany)
XML	Extensible markup language
CNS	Central nervous system
Δ9-THC	Delta-9-tetrahydrocannabinol

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